T H E S I S

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<u>T H E</u> <u>M A L P I G H I A N</u> <u>B O D I E S</u> <u>O F</u> <u>T H E K I D N E Y</u> .

A STUDY OF THEIR DEVELOPMENT, COMPARATIVE ANATOMY, AND PATHOLOGY.

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Presented by

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for the Degree of

M.D.

and as a competitor for the Goodsir Memorial Fellowship.
& Gunning Prize in Pathology.

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INTRODUCTION.

The following Thesis which I have the honour to submit for the degree of Doctor of Medicine, and as a candidate for the Goodsir Memorial Fellowship, comprises the results of part of my work in the University Pathological Laboratory as a Crichton Research Scholar.

I have the greatest pleasure in expressing my sincere thanks and indebtedness to Professor Greenfield, not only for his suggestion of the subject of my work, but for the many facilities he has given me for carrying it out in his Laboratory.

Though originally intended to deal with Pathological changes only, the Thesis is chiefly a study of the Development of the Malpighian bodies of the Kidney. A knowledge of their minute Anatomy and Development was necessary to follow out certain changes that occur in disease, and on looking up the literature of the subject I was surprised to find that very little was known about their Development, that most of the work had been done by German observers, and that their results were very contradictory. I had the good fortune to secure a number of Human Foetal kidneys, and have examined them very carefully. The results are here stated, and a record of many of the different stages in Development are shown in Photomicrographs. This is as far as I am aware the first time that photographs of the subject have appeared, the usual diagramatic drawings which are given as illustrations being made to order to suit any theory. The Development of the Malpighian bodies included a number of other closely related structures which could not be omitted; the Development of the Malpighian bodies really constitutes the greater part in the History of the Development of the whole Kidney.

In addition a Section has been added on Comparative Anatomy and Embryology in which the Malpighian bodies of the different orders of Vertebrates are compared. A few of the more interesting types are recorded among the Illustrations.

The Section on Pathology had to be shortened and a quantity of experimental work omitted.

To Professor Simpson and Dr. Halliday Croom my thanks are due for their kindness in allowing me Embryological material from the Royal Maternity Hospital. To the late Professor Rutherford I owe a debt of gratitude for the help he gave me at the commencement of my research. I must also express my thanks to Dr. Welsh for his kindness in furnishing me with Pathological specimens and many valuable suggestions.

The Illustrations of the Thesis have been enclosed in a separate cover to lessen the bulk of one volume, and to allow of more convenient reference from the text. The Photomicrographs have been prepared by Mr. Richard Muir, to whom I am deeply indebted for his excellent reproductions of the microscopic appearances, and for the help he has given me throughout my work in the Laboratory.

The slides + microscopic specimens have been left under the care of Professor Greenfield in the Pathological laboratory of the University. If necessary they can be obtained from him.

A short Historical Survey of the Anatomy of the Malpighian bodies of the Kidney.

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HISTORICAL SURVEY OF THE ANATOMY OF THE MALPIGHIAN BODIES OF THE KIDNEY.

Our knowledge of the Malpighian bodies of the Kidney may be said to date back to the end of the 17th century.

Malpighi the great Italian anatomist described them in this work "De Renibus" published about the year 1688, and ever since then they have borne his name. Malpighi regarded them as internal glands of the Kidney concerned in the elaboration of urine from the blood. He recognised that they were mainly vascular structures, and also believed that each was the starting point of a urinary tube.

During the next century little further was known about them till Ruysch injected the renal artery, and found that the injected material accumulated in the Malpighian bodies, which were thus rendered conspicuous to the naked eye. Ruysch and other later observers, who followed the same plan of injecting the renal artery, often noticed that the injected material escaped from the Malpighian bodies along the urinary tubules. From this they were led to conclude that there was a direct connection between the lumen of the blood vessels and the urinary tubules, an error which was one of the foundations for the belief in exhalent arteries.

Very little was known about their structure and function, even in the beginning of the present century, for we find Huschke in 1828 and Müller in 1830 advocating the view that the Malpighian bodies were structures lying among the urinary tubes but quite independent of them.

In 1842 Bowman (Bb.6) read his remarkable paper "On the Anatomy and Physiology of the Kidney" before the Royal Society. By it our knowledge of the Anatomy and Physiology of the Kidney was raised at one bound from a state of ignorance to a level very little exceeded at the present day. Bowman showed that the Malpighian body was the dilated extremity of a urinary tube, in which hung a number of capillary loops. The outer wall or capsule of the Malpighian body he believed to be merely an expansion of the basement membrane of the tubule, and this outer wall is now known as Bowman's Capsule. Bowman considered it to be a simple homogenous and transparent membrane in which no structure could be discovered. He laid stress on the fact that it was never reflected over the vessels, but allowed them to penetrate it opposite the beginning of the urinary tube. Bowman examined the kidneys of many different animals and found that there were great varieties in the way the capsule was lined. In many cases he found a lining of epithelium extending over the whole inner surface of the capsule, but in others he could not detect the slightest appearance of it over more than one third of the capsule. In the frog he noticed that the cells lining the neck of the capsule were ciliated, but when fairly in side the capsule the cilia disappeared, and the epithelium beyond was of excessive delicacy and translucency, nuclei were seldom present and the cells had a great tendency to swell up on the addition of water. Bowman showed that the vascular portion of the Malpighian body consisted of an afferent arteriole which penetrated the basement membrane and broke up into a number of capillary loops, which after forming festoons inside the capsule, united to form a single trunk the efferent arteriole, which again penetrated the capsule close to the entrance of the afferent vessel. He believed that the capillary loops forming the Glomerulus hung free inside the capsule, each capillary having a wall consisting of a simple homogenous and transparent membrane. Bowman insisted particularly on this that there was no reflection of the capsule over the capillaries, and no other tissue admitted into the capsule besides blood vessels. By the careful injection of the renal artery he further pointed out how Ruysch and others had been led into error owing to their having employed too great a pressure, thereby rupturing the capillaries inside the capsule, and forcing the injected material along the tubules.

Bowman's paper was soon criticised by a number of German observers.

Gerlach (Bb 21)in 1845 showed that the capillary tufts were not naked in the capsule as Bowman had declared. Gerlach described a single layer of flat epithelium covering the tuft and continuous at the base with the epithelium lining the capsule.

Kölliker (Bb.46)shortly afterwards found the same, and further showed that the membrane of epithelial cells which covered the tuft, dipped down into the spaces between the capillaries, everywhere separating them from the cavity of the urinary canal.

Bidder (Bb.4)in the same year described a partition of fine epithelium covering the Glomerulus , and continuous at its base with the tunica propria.

Remak (Bb.64)in 1855 described the development of the Kidney. He considered that the Malpighian body was formed by an invagination of the end or one side of a urinary tubule by the ingrowth of bloodvessels. According to Remak therefore the epithelium lining the convoluted tube and Bowman's capsule, and that covering the capillaries were continuous structures, originally the same, but altered during the further process of development.

Schweigger Seidel (Bb.75) in 1865 laid stress on the fact that during the development of the Kidney, the epithelium covering the glomerulus consisted of large cells which covered and penetrated between the capillaries. The presence of such a marked layer of cells in the foetus, he argued, implied the existence of a continuous layer of cells in the adult.

Heidenhain (Bb.34) also drew attention to the way the membrane dipped down between the capillaries, dividing the Glomerulus into lobules.

Many other observers demonstrated this epithelial investment of the glomerulus and its presence has been universally admitted. Of the blood vessels composing the glomerulus, Bowman showed that there was usually a single afferent and a single efferent artery, the afferent being slightly larger and having a thicker wall than the efferent. The afferent artery breaks up into from four to eight branches, (Ludwig (Bb) 52), immediately after entering the capsule, and these form capillary loops. Besides capillaries

Ryndowsky (Bb72) has described lymphatic vessels in the glomerulus, and many believe in the presence of a certain amount of fine connective tissue lying between and supporting the capillaries. The structure of Bowman's capsule is not fully settled. Bowman believed it to be a homogenous membrane, and this is the view generally adopted. Ludwig (Bb52) considered it to be a mosaic of cells closely resembling those composing the wall of the blood and lymphatic capillaries, and Roth (Bb69) thought it to be made up of endothelial cells. Recently in 1897 Rühle (Bb71) has stated it to be composed of thin fibrils, and he has described its continuation into the glomerulus as a fine thread like structure with numerous pores.
In the foetus it is indistinguishable, the wall being in many cases apparently formed by the surrounding connective tissue. In old age it becomes marked and appears to be as Bowman described it, a simple homogenous membrane.

The cells lining Bowman's capsule are continuous as Bowman showed, with the cells lining the convoluted tubule, and vary in character in different animals.
Some of these variations will be treated of later on. From a consideration of the development of the Malpighian bodies, the cells lining Bowman's capsule

and those covering the glomerulus have been regarded as part of the epithelium of a urinary tube specially differentiated for the performance of a different function. But sufficient stress has not been laid on the fact that they differ not only from the cells of the tubules but from one another.

It is to the alterations that take place in disease that we have to turn for further information; in the normal adult kidney the anatomical appearances of the cells is very similar, but in many forms of disease alterations in structure take place, which give us a clue to their real significance. It is found that the cells lining Bowman's capsule react in quite a different manner to those covering the glomerulus. The latter have more of the nature of glandular cells elsewhere, but the cells lining Bowman's capsule react not as a glandular epithelium but very much the same as the cells lining the inner wall of an artery. Professor Greenfield in his Resume of Renal Pathology, published in the New Sydenham Society's Atlas in 1879 described the cells lining Bowman's capsule as closely resembling those which form the endothelium of blood vessels, and pointed out that in many forms of Nephritis they proliferated and gave rise to organised fibrous tissue which eventually compressed and obliterated the glomerulus.

It seemed contrary to generally accepted ideas that a glandular epithelium should behave in this way, and to arrive at the explanation I was led to study the development of the Malpighian bodies. The most recent accounts of this stated that the epithelium of the Malpighian bodies was derived from the Wolffian duct, which is now believed to be Epiblastic. That Epiblastic cells should react in disease like the endothelium of an artery seemed more unlikely still. On further investigation I found that the views on development were most conflicting, and that really little was known.

I have gone carefully into the development and have also made some observations on the Comparative Anatomy of the Malpighian bodies. These are recorded in the following sections.

THE DEVELOPMENT OF THE HUMAN KIDNEY

WITH ESPECIAL REFERENCE TO THE

MALPIGHIAN BODIES.

DEVELOPMENT OF THE HUMAN KIDNEY.

In the Kidney of man and the higher Vertebrates the origin of Malpighian bodies is so closely related to the origin of other structures, and their further development plays such an important part, that it is necessary to consider some of the main facts of the history of the development of the whole organ.

The development of the kidney has been worked at by a great number of Embryologists, but most of the observations have been made on embryos of the higher Vertebrates other than man, especially on those of the chick, rabbit, dog and pig. That there is a close similarity between the histories of development of the kidneys in these animals is a fact generally admitted, and the different results recorded by different observers are not to be explained by the difference in material examined. My own observations have been made for the most part on the kidney of the Human embryo, and all the photo-micrographs in this section are from the Human kidney. I have also examined the developing kidney in the chick and the mouse, and find in them a close resemblance.

The Kidney of man corresponds to the Metanephros of comparative anatomy, which is the most highly differentiated of the urinary organs of Vertebrates. In the embryo there is at an early stage a well developed Mesonephros which for a time appears to be the functional excretory organ. According to Marshall (Bb.55.) the Mesonephros or Wolffian body begins to form about the 18th day of intra-uterine life and attains its greatest development at the end of the 8th week, after which it atrophies and is replaced by the permanent kidney.

The presence of a Pronephros or Head Kidney in the Human embryo is doubtful. Janosik (Bb.40.) has described one in an embryo 18 days old. Marshall says of it, that if present at all it must be extremely rudimentary and evanescent.

The Wolffian body is generally admitted to be derived from the Mesoblast, either of the Intermediate cell mass, Sedgwick (Bb.76.), or the peritoneal epithelium Braun, (Bb 9.), as segmentally arranged strings of cells which acquire lumens, and at a later period open into the Wolffian duct. Waldeyer (Bb.87.) on the other hand believed that the Wolffian body was an outgrowth from the Wolffian duct. Braun and Kölliker (Bb.45.) were of the opinion that each of the Wolffian tubules was derived from peritoneal epithelium, and that at an early stage they opened at one end into the body cavity. This opening was denied by Fürbringer (Bb 20.). Sedgwick denied that the peritoneal epithelium was the chief factor in their formation, and gave as their origin the cells of the Intermediate Cell mass. Balfour (Bb 2.) believed that they arose independently of the Wolffian duct, but that their history varied in different animals. In the lower Vertebrates e.g. in Elasmobranchs they were formed from the intermediate cell mass, but had peritoneal openings from the very first. In the Amniota there was no attachment to peritoneum.

The Malpighian bodies of the Mesonephros are formed at the end of the tubules, and are therefore derived from the peritoneal epithelium or intermediate cell mass, if we accept the opinion of the majority of these authors.

The Wolffian duct is the functional excretory duct of the Mesonephros, and is believed, as above stated, to have an origin independent of the Wolffian body. Owing to the important part it is said to take in the later formation of the Metanephros, mention must be made of some of the views regarding its formation. The older Embryologists, and especially Balfour (Bb 2.), held that it was a Mesoblastic structure. In the lower vertebrates the development of which Balfour studied particularly in Elasmobranchs, he found that the Wolffian duct arose from the Segmental duct, which was formed from Mesoblast. Of the Urino-genital organs in Vertebrates Balfour said, "Whatever may have been the primitive origin of the system, its Mesoblastic origin in Vertebrates cannot in my opinion be denied." (Bb. 2.).

Recently the view has gained more general acceptance that the Wolffian duct is formed from Epiblast. The study of its origin in the human embryo is rendered difficult by the impossibility of acquiring suitable specimens. Kollmann(Bb. 47.) has described its formation in a human embryo about a fortnight old. He found a pair of longitudinal grooves in the Epiblast, which he considered formed a solid column of cells, and described them as becoming detached about the 3rd week from the remaining Epiblast, and sinking into the Mesoblast of the Intermediate Cell masses. About the same time a lumen was formed. Schäfer (Bb. 74.) considers it to be an Epiblastic structure. On the other hand Marshall is in favour of its being Mesoblastic in all animals.

The Ureter arises from the dorsal aspect of the Wolffian duct near its hinder extremity. This was described by Kupffer (Bb. 48.), and has been confirmed by numerous observers. The origin of the tubules of the kidney has been a matter of much dispute, and there have been for many years, and still are, two distinct opinions.

The older opinion and one that has received the more support is, that the kidney tubules arise as continuous outgrowths from cells in the pelvis of the kidney, which have been originally derived from the Wolffian duct through the outgrowth of the ureter. In other words, that they are branches of the ureter, which is in turn a branch of the Wolffian duct. According to the advocates of this view all the tubules of the Kidney including the epithelium lining Bowman's capsule and that covering the Glomerulus are derived from cells, which were originally part of the Wolffian duct. They are therefore to be regarded as Mesoblastic or Epiblastic according as we regard the origin of the duct as Mesoblastic or Epiblastic. If the cells lining Bowman's capsule be derived from Epiblast we can scarcely consider them as likely to assume the characters of endothelium.

The alternative view of the development of the glandular portions of the kidney is that they arise independently of the ureter and its branches, and only unite with these at a later stage. The kidney is supposed by the advocates of this view to develope in a manner similar to the Wolffian body. The supporters of both opinions allow that the Ureter and Collecting tubes are branches which arise in continuity from the Wolffian duct. The difference then is one with regard to the origin of the Malpighian bodies and tubules beyond the Collecting Tubes.

The first clear account of the development of the kidney appears to have been given by Remak (Bb.64.) in 1855. He traced it in the embryo of the chick, rabbit, dog, and cat, and described columns of cells which grew from the pelvis to the cortex and formed the urinary tubes. His description of the formation of the Malpighian body led to the common belief that it consisted in the invagination of the wall of the end of a urinary tube by an ingrowth of capillaries. Remak described the end of one of the epithelial columns curving round what afterwards became the Glomerulus, and which by its further growth formed a basin shaped invaginated swelling either at the end or in a side wall of the tube. Remak considered that the epithelium covering the tuft was a continuation of the membrane propria of the tubule.

Before Remak other observers Burdach (1828) Müller (1830) and Rathke (1833) are quoted by Hamburger (Bb. 29.) in a recent paper, as having expressed the views that the tubules of the kidney arose as buddings from the Ureter branches.

Waldeyer (Bb 87.) and Toldt (Bb 84.) were strongly of the opinion that all the tubules of the kidney were developed from the Ureter. Kölliker (Bb 45.) described the same. Löwe (Bb 57.) described all the tubules as arising from the ureter but believed that the Glomerulus arose as an independent structure in the cortex.

Pye (Bb 61.) and Ribbert (Bb 65.) described the formation of the Malpighian bodies very carefully. They both considered that the Collecting tubules each ran from the pelvis to the cortex of the kidney and immediately under the capsule bent completely round with a short end which developed into Malpighian body, Convoluted tubules, and Henle's loop. All were therefore branches of the ureter, and in continuity from the very first. With these observations most of the later authors agree. Hortolès (Bb 37.), Golgi (Bb 24.), Nagel (Bb 57.), and Berry Haycraft (Bb 32.), all consider the different parts of the tubules, and Malpighian bodies to be in continuity from the very first, and to arise as outgrowths from the ureter.

The second view that the glandular portion of the kidney has an origin independent of the Ureter has also received considerable support. Thayssen (Bb 83.) was the first to definitely state the opinion that the Collecting and Junctional tubules were formed as hollow buds from the ureter, while the Malpighian bodies and their appertaining Convoluted tubules and Henle's loops were developed independently from solid masses of cells in the "Nierenanlage." Each Malpighian body arose from a solid mass of cells in which a split like lumen appeared, a description very different to that given by Remak and Toldt. Thayssen did not describe the union of the two systems.

Riedel (Bb 67.) described a very similar process. He showed that the Malpighian body was a solid mass of cells, which developed a lumen continuous with the Convoluted tube. He further described the union of the two systems; the Collecting tubule ended under the capsule in a dilated vesicle the Ampulla, which gave off a side branch to join the developing Convoluted tubule. In this way all became continuous with the ureter.

Bornhaupt (Bb 5), Braun (Bb 9.), and Furbringer (Bb 20.), agreed in the main with Thayssen and Riedel, that the Malpighian bodies and secreting tubules arose from Mesoblast, and united with the Collecting tubules at a later stage.

Braun considered that in Lizards the cells which gave rise to the Malpighian bodies and secreting tubules were developed from irregular strings of peritoneal epithelium. Fürbringer believed them to be differentiations of the dorsal tubules of the Wolffian body. Sedgwick (Bb 76.) while admitting their independent development, denied that they were formed from peritoneal epithelium, but described a blastema of cells in the chick continuous in front with the blastema of the Wolffian body. The kidney blastema as well as the blastema of the Wolffian body, he believed to be developed from the mesoblast of the Intermediate cell mass. Hamburger (Bb 29.) 1890 is the latest observer who has described fully the separate origin of the secreting portion of the kidney. Schäfer takes the same view in the Embryological portion of Quain's text book of Anatomy, and states that the Malpighian bodies, Henle's loops and the Convoluted tubules arise from portions of the Intermediate Cell mass, which are situated posterior to the Wolffian body. This is practically the same as Sedgwick described. Hamburger worked at the development of the kidney tubules principally in the mouse. His description agrees with that given by Thayssen, but is more minute.

The figures illustrating his paper are very diagrammatic, and with some of them I find it impossible to agree, but on the whole my own observations have led me to conclude with this group of authors, that the two systems arise independently, and are not continuous structures from the very first. To avoid errors in illustration I have selected examples of different stages in the process, and record them in the Photomicrographs appended.

Unfortunately I have not been able to obtain specimens of the human kidney at its earliest stages, but have examined many from the third month onwards. As the process of formation of new Malpighian bodies and tubules goes on up to the time of birth, and during that time the processes are similar, it is quite reasonable to suppose that the same takes place before the third month. It is very unlikely that the first Malpighian bodies are outgrowths from the ureter and that subsequently the remainder which form a vast majority, develope independently of the ureter. The tissue surrounding the ureter branches which gives rise to the Malpighian bodies has been shown by numerous observers to be present from the very first, and is formed according to the later authorities from the mesoblast of the intermediate cell mass.

Before passing to the mode of formation of an individual Malpighian body and its tubule, it is necessary to state shortly a few facts concerning the early history of the development of the kidney.

The ureter is said by Marshall (Bb 55) to begin to form about the early part of the 4th week of intra-uterine life. A budding of the hinder end of the Wolffian duct takes place to form a solid column of cells, which gradually grows forward until its anterior end occupies the position of the pelvis of the future kidney. In the chick Sedgwick has shown that the kidney blastema closely invests the anterior end of the ureter. Kőlliker (Bb 45) described in a human embryo of 8.5 mm long the kidney as a single club shaped structure connected by a straight canal with the sinus urogenitalis. Its club shaped anterior end was surrounded by a thick accumulation of mesoderm cells. Kőlliker believed that this mesodermic investment gave rise to the blood vessels and connective tissue of the kidney. Phisalix (Bb 60.) showed that in an embryo 10 m m long the kidney consisted of a cylindrical sac with widened lumen surrounded by a dense mass of mesoblast.

Schäfer describes a similar investment, and states that it is derived from the intermediate cell mass.

All observers are agreed that the pelvis of the kidney is formed from the anterior dilated extremity of the ureter, and that from it branches arise which form the calyces and collecting tubules. The branches are at first solid but acquire lumens. The distal end of the ureter at the same time becomes detached from the Wolffian duct and opens into the Urogenital sinus.

Great importance has been attached by the German writers to the cells which line the pelvis of the developing kidney. According to the first group of authors mentioned they give rise to all the tubules of the kidney, while others only allow that they form the collecting, and perhaps the junctional tubules. In the human kidney at the middle of the third month, the cells lining the pelvis and occupying the position of the papillae, have the following characteristics. Each cell is cylindrical, and from two to three times as long as it is broad. They are usually arranged in columns of two cells deep with a central lumen, in other places they form masses of considerable size especially at the apices of the papillae. Where there is a lumen it is narrow, and the margins of the cells forming it are flat and continuous. The opposite ends of the cells are tapering, and between them are placed the tapering ends of the cells in the deeper layer, the broad ends of the cells of the deeper layer are therefore outermost, and present a regular border, but do not seem to have a definite basement membrane, but are closely surrounded by embryonic connective tissue and blood vessels. Each cell has an oval nucleus with one or two deeply staining granules. The nucleus is nearer the broad extremity of the cell, and the protoplasm is large in amount and stains very lightly. As the columns approach the cortex they grow less in size and divide dichotomously, the cells form a single layer, and become shorter, with the nucleus relatively larger, and placed deeper in the cell. In the cortex each tubule has a well marked lumen, the cells are cubical with a larger and more deeply staining nucleus, and relatively little protoplasm. The tubules run fairly straight in a radiating manner towards the cortex, divide dichotomously once or twice and end in dilatations, the so called Ampullae, immediately under the capsule. The appearance of each Ampulla varies at different stages, and will be described more fully in connection with the formation of the Malpighian bodies. It is of great importance and constitutes the growing end of the collecting tube, and is the part with which the convoluted tubules unite. The Pyramids or Renculi appear to be formed early, and each is represented by a mass of the cells above described. From these masses of cells spring the collecting tubules, each of which gives origin to the primitive cone of Ludwig. At this early stage there is no great difference between cortex and medulla, and the earliest Malpighian bodies are found among the collecting tubes close to the pelvis.

The lobulation of the kidney is not well seen at first, but becomes more marked during further growth. In the third month the kidney is a flattened elongated body with an indentation at the Hilum where the ureter enters. In the 5th and 6th months lobulation becomes marked, the number of lobules varying with the number of pyramids, usually about sixteen, but varying from eight to twenty. From the 7th month onwards the lobulation becomes less marked, but can still be traced for some time after birth.

The relation of Malpighian bodies and convoluted tubules to the collecting tubules would seem at first sight to be a simple matter to decide, but it is really a most difficult question, as the different opinions of skilled observers show. Before discussing it, the methods that have been employed in investigation may be noticed. Some of these are obviously misleading. The earlier observers examined sections, but owing to the imperfect means of cutting them sufficiently thin, could not appreciate the fine distinctions necessary to establish the independence of structures. Their method of staining was also imperfect. Ribbert (Bb 65) in his paper on the development of the Malpighian bodies in 1880, laid stress on the fact that their development was more easily traced in the kidneys of older foetuses where the connective tissue was not so abundant. In the very young kidney he found the connective tissue cells so numerous and staining so like the cells of the tubules, that he could not distinguish between them. I am convinced that this was the reason of his description of the tubules being continuous structures, because he examined specimens in which the tubules had already united.

Many observers have made Isolation preparations by various methods of maceration and teasing the tubules from their surrounding connective tissue. Hamburger used this method in conjunction with serial sections, but found it to be impracticable in the very young kidney owing to the large amount of connective tissue.

The condensed layer of mesoblast under the capsule renders isolation impossible, and even in the later stages when the tubules have united they are very fragile, and often break even when cut in section as may be seen in Fig. (11.). The cells which form the Malpighian bodies and convoluted tubules are at first indistinguishable from the connective tissue cells, and could not be isolated from them. Colberg (Bb 13.) injected the blood vessels with coloured material, this is recognised to be of very little use in newly formed and forming tissues. Under the capsule there are few capillaries formed, and those already formed are so delicate that rupture of their walls is inevitable. The capillaries of the glomerulus are not formed at first, and do not push in the wall of a tubule in the way described by Remak and Toldt. This may have led Colberg to give the name of "Pseudo-glomeruli," to structures which are really Malpighian bodies at an early stage before the formation of capillaries in them.

The only reliable method of examination is by the careful preparation of a series of thin sections. The tissue examined should be well fixed and hardened, and cut in paraffin.

The sections best adapted for the purpose are those cut parallel to the collecting tubules, longitudinal sections through the widest portion of the kidney including the pelvis show the most detail. Transverse and tangential sections should also be made. Owing to the tortuosity of the convoluted tubules even at an early period, it is difficult to obtain a section in which a continuous lumen appears, but the examination of a consecutive series of sections shows whether they are continuous or not. The method of serial sections has been made use of by most of the later observers, and their results are conflicting. The method is tedious, and often difficult, but seems to be the only satisfactory one. Of staining reagents I have tried many, and find Heidenhain's Iron alum Haematoxylin method gives the best results. By it there is a greater differentiation between the different structures than by any other method I have tried, it is also very suitable for photographic work. A counter stain of Rubin and Orange improves the appearance of the section, and is of value in staining the cells of the convoluted tubules when they have become well developed.

The presence of dilated spaces lined with epithelium in the cortex of the developing kidney has long been known. Valentin (Bb 85.) in 1835 described club shaped structures from which he believed both cortex and medulla were formed. They are the "Ampullae" of the German writers, and have long been recognised as the peripheral ends of the ureter branches, or future collecting tubules. They are situated almost immediately under the capsule, or close to the interlobular septa, and often show a dichotomous division. In some animals the branches from the Ampullae are more numerous. I have never seen more than two in the human kidney. The cells forming the wall of the Ampulla are arranged in a single row, and are cubical in shape, with large deeply staining nuclei. They are sharply defined from the surrounding tissue, and during the process of hardening often shrink from it, leaving a space. Toldt (Bb 84.) described the cells of the collecting tubes as forming by proliferation solid cells cones, which at a later stage became hollow, and gave rise to the convoluted tubules. Ribbert (Bb 65.) showed that each Ampulla divided into two branches, which curved round under the capsule, then descended parallel to the ascending tube. The descending limbs were short, and soon became curved, a Malpighian body forming in the hollow of the lowest curve. The lumen was continuous throughout. But Ribbert examined the kidneys at a late stage of development, generally about the time of natural birth, and his description is quite true of that stage, he apparently did not see the earlier stages.

Golgi appears to have described the process very fully. (Bb 23.) (Unfortunately I have been unable to obtain his* paper). His diagram of the development of the urinary tubules appears in almost all the text books. He apparently believed in the division of the collecting tube into two branches under the capsule, each branch curving round and descending in the manner described by Ribbert. Other observers have come to the same conclusions. Berry Haycraft (Bb 32.) in 1895. All the foregoing authors have figured in diagrams a stage which does exist, but is a comparatively late one. Fig. (11.) shows the continuity of Malpighian body convoluted tube and collecting tube almost diagrammatically, and is very similar to Golgi's diagram. Almost all have noted the dense layer of mesoblast which surrounds the Ampullae. Ribbert found it too dense in the young kidney for a satisfactory examination. Remak, Toldt, and Schweigger Seidel, recognised the large amount of connective tissue, and believed it was formed from the dense layer under the capsule.

Thayssen (Bb 83.) was the first to bring into prominence the view that the Malpighian bodies, and convoluted tubules were not branches from the collecting tubule, but were formed in close proximity to it from the layer of condensed mesoblast. Other observers came to a similar conclusion. Riedel (Bb 67.) gave a more complete description of the process. He showed that a layer of mesoblastic cells surrounded the ureter branches, and as the kidney grew, remained in the periphery of the lobules, and formed masses of epithelial cells closely surrounding the Ampullae, but distinctly separate from them. In the masses of cells thus developed lumens appeared, and at the same time they became continuous with the collecting tubes. Braun (Bb 9.), Bornhaupt (Bb 5.), Sedgwick (Bb 76.), Balfour (Bb 2.), and others were convinced that the Malpighian bodies and convoluted tubules arose independently of the Ureter branches. Of late years the opposite view has received the most support, and agreeing with Thayssen we only find Hamburger (Bb 29.) 1890, Schäfer (Bb 74.), and Hertwig(Bb 35.).

My own observations led me at first to believe that all the kidney tubules were branches from the collecting tubes, but I could never find the early stages which should have been easily seen if that view were correct. In the thick layer of the capsule, cells are seen which show a gradual transition in appearance from embryonic connective tissue cells to a character closely resembling that of the epithelial cells of the early convoluted tubules. Between these cells and those of the Ampullae there is always a distinct line of separation, and in the majority of instances there is a space, where the tubule has shrunk during the process of hardening. The careful examination of serial sections has convinced me that these masses of cells which appear under the capsule, and in the interlobular septa, are quite independent of the ureter branches, and give rise to Malpighian bodies, convoluted tubules, and Henle's loop, uniting always with a short branch from the Ampullae.

The cells which form the layer under the capsule, and constitute the interlobular septa, are very numerous; those on the surface of the capsule, and in the middle of the septum, are elongated with long drawn out nuclei, and are arranged with their long axes parallel to the surface of the lobule. They are thus arranged for several layers, but as they lie deeper they become rounder and larger. In the deeper layers the cell outlines are difficult to see, there is little protoplasm, and the nucleus is large, round or oval and deeply staining. Over the Ampulla the cells take up an arrangement very like a cap fitting on its extremity. A transition in character between the cells can be seen. It is illustrated in Fig. (3.) which shows a very common appearance. The cells next the Ampulla are becoming arranged in a layer which is distinctly separated from it, the cells in this layer are almost columnar with large oval nuclei. In fig. (3.) two collecting tubes are shown ending in dilated extremities, the Ampullae. Over the end of each Ampulla lies a cap of cells as described above. Note the sharp line of demarcation between tube and cap, which is here emphasised by the contraction of the cells of the tubule during the process of hardening. Between the capsule and the cap there is not a similar distinction, the cells gradually change in character from the one to the other, and it is difficult to say where the one begins and the other ends. The further development of this cap of cells clearly shows that they become epithelial in character, the difficult question to decide is, whether they are continuous with the epithelial cells of the collecting tube, or whether they are independent structures arising from the mesoblastic covering under the capsule. Toldt (Bb 84.) regarded them as solid cones, which were thrown out by the collecting tubes, and pushed their way through the condensed connective tissue as fingers through a glove. On examination of sections one always finds a well marked line of separation between the Ampullae and the caps or cones of Toldt. In no case have I seen them continuous, and the distinction is well seen in several of the Figures. The cells of the two structures also differ in character. An early stage is seen in Fig. (3.), the cells nearest the Ampulla become elongated and arranged with their bases towards the tube, the more superficial layers remain composed of ordinary embryonic connective tissue cells. Gradually more cells become elongated with larger nuclei until a mass of cells has been formed over the Ampulla several layers deep. Fig. (4.). A second line of demarcation then begins to appear on the other side of the cap between it and the connective tissue, a definite mass of cells is thus formed, which lies over the end of the Ampulla, and is definitely marked out from its surroundings. Fig. (4.). Berry Haycraft (Bb 32.) believed that the appearance was due to the end of the tube having been cut obliquely, and that the two structures were really continuous. In Fig.(5.) the Ampulla has been cut obliquely, and as a consequence there are a number of cells at the end of the tube which really are part of the wall, but which being cut obliquely, looks as if they formed a solid mass. But quite separate from this mass of cells is another under the capsule, the beginning of another convoluted tubule and Malpighian body.

The two structures in this Fig. cannot be said to be a continuation, and appearing solid because cut obliquely. The difference between the cells of the cap, and those of the Ampulla are here well seen. The cells in the cap take on a much deeper stain, their nuclei contain more chromatin than the nuclei of the cells of the tubule, and show evidence of active growth and division. If it be granted that the two structures are not continuations in the Figs. there remains still the possibility that the cap may be an out growth from some other part of the collecting tube, the side wall for instance, and the appearance may be due to its subsequently having curved round the end of the Ampulla. I have examined serial sections very carefully, and find no indication of this being the case, in all, the cap appears to be a separate structure at this early stage. In the later stages there sometimes seems to be a connection between the mass of cells after a lumen has begun to appear and the cap which is in process of formation. This is only what one would expcet, the cap in this case becomes detached from the mass of cells with the lumen, and is the origin of another system, the two are different stages of development of two separate tubules, but both belong to the same primitive cone, that is, both open into the one collecting tubule.

In Figs.(4. + 5.) one might suppose that the cap was really another collecting tubule curving round under the capsule in the way described by Ribbert, and that it appeared solid because the section was one cutting through the side wall all the way. Examination of serial sections proves that this is not the case.

I am strongly of the opinion that the cap of cells which appears over the end of each collecting tubule is a structure independent of that tubule, and further that it give rise to a Malpighian body, convoluted tubules, and Henle's loop.

Emery (Bb 17.) described a similar origin. He used only the method of serial sections, and found that there appeared a Cell group between each Ampulla and the capsule. From this Cell group there developed a "vesicule renale" which was separated from the collecting tube by a sharp contour, and only united with it when the Malpighian body began to form.

Hamburger (Bb 29.) came to the same conclusion. He described the collecting tubules ending in Ampullae under the capsule, but separated from it by a "Zellschicht" or "Zellmantel". The cell mantle was composed of cells with round or oval nuclei, which were more deeply stained by carmine than the nuclei of the cells of the surrounding connective tissue, and it was always separated from the Ampulla by a sharp contour. By following their relations through a number of serial sections he was convinced that "No Continuity existed at any point between the "Anlage" and the Ampulla". The "Anlage" gave rise to the "geschlangelten Röhren", each of which became united to the Ampulla by one end, while at the opposite end there developed a Malpighian body.

The layer of cells in which these Caps or Cell mantles appear is confined to the periphery of each lobule, it follows therefore that new Malpighian bodies and convoluted tubules only develope in the periphery. It is not correct to say that they develope only under the capsule, because they form in the interlobular septa as well. The Mesoblastic covering of the ureter branches is a structure of great importance. In the third month it forms a fairly even surface under the capsule, but portions of it are continuous between the first branches of the Ureter. As the collecting tubules grow and become arranged in groups, each group giving rise subsequently to one lobule, the covering remains at the peripheral ends of the tubules. Lobules are gradually formed, the cellular covering being still at the periphery of each. With further growth the lobules coalesce from the pelvis outwards, the capsule becomes continuous at the point of junction of one lobule with the other, but the cellular covering or "Anlage" of the German writers remains between the lobules, and dips down from the capsule to the pelvis. Figs (1.+2.) show the lobulation. In Fig (1.), which is a section of a human kidney at the 4th month, lobulation is not marked on the surface, but the division by septa internally can be seen. Fig (2.) from a human kidney at the 6th month shows a single lobule which is made up of cortex and medulla. The capsule on the surface bridges from one lobule on to the next, leaving a wedge shaped space between their surfaces, which is filled with loose connective tissue. There is a distinct line of separation between each lobule extending from the capsule to near the pelvis. This line of separation is composed of a dense mass of mesoblastic cells, and is really a double layer of the same nature as the layer under the capsule. Each lobule has its own layer, and they can be seen to blend where the two surfaces come together at the point of the wedge shaped space between the lobules. In this mesoblastic septum the central cells have a longitudinal direction as under the capsule, but on either side they become larger with round deeply staining nuclei, and among them appear the cells mantles or caps in relation to the Ampulla just as under the capsule. Malpighian bodies and convoluted tubules therefore develope in the periphery of each lobule on either side of the septum.

In addition to glandular elements, there is a large amount of embryonic connective tissue in the foetal kidney. It is more abundant and cellular at first, and gradually decreases towards the time of birth. The largest amount is found in the cortex, where it is difficult to distinguish it from the cells which give rise to the tubules. The connective tissue of the kidney is recognised by all to be formed from the mesoblastic covering of the ureter branches. Remak, Kőlliker and others considered that the branches of the ureter grew into the connective tissue, and that there was a constant proliferation of connective tissue and tubules under the capsule. The connective tissue certainly appears to be formed under the capsule, and the question arises, "Are both connective tissue cells and epithelial cells developed from the same layer?" This is a difficult matter to decide. The superficial layers under the capsule consist of flattened cells with a longitudinal arrangement, these appear to be definitely part of the capsule. But below them the cells are very thickly massed together and resemble one another in appearance. Cŏllecting tubules reach the periphery of the lobule at numerous points with small intervals between. Over the Ampullae the cells take up the arrangements already noticed, but in the intervals the cells become less numerous, their nuclei elongate, and many take up an arrangement with their long axes parallel to the collecting tubules. This flattening of cells is sometimes marked round the outer side of what becomes Bowman's capsule. The majority of the cells between the tubules develope into mucoid tissue, they become less numerous from the cortex to the pelvis, and in the deepest layers consist of large branching cells, with small nuclei. They are most numerous in the young kidney, and are very plentiful at the 3rd and 4th months, but with the further growth of the kidney they gradually disappear but not entirely. Hortolès (Bb 37.) commenting on the large amount of connective tissue in the foetal kidney, said, that though it for the most part disappeared it still existed "en puissance" throughout life, and was rendered evident by pathological processes. Connective tissue is always evident in the papillae between the collecting tubes, and remains so in adult life. Most of it disappears from the cortex, but some remains under the capsule, and to a less extent in the positions of the interlobular septa. Delicate connective tissue can often be found around the larger blood vessels, and surrounding the Malpighian bodies. The presence of a definite arrangement of connective tissue in the adult kidney was first pointed out by Goodsir in 1842 (Bb 25.). Goodsir described a fibro-cellular framework pervading the whole gland, and compared it to Glisson's capsule in the liver. This framework is not very evident in the healthy adult kidney, but becomes a great feature in some of the chronic inflammatory lesions. Goodsir's description is especially true of the foetal kidney, in which the framework is cellular and large, forming separate compartments for each tubule.

Among the connective tissue of the cortex of the developing kidney numerous capillaries are formed. These appear to me to be developed in situ, and not as outgrowths from the larger vessels. Some of the mesoblastic cells become more and more elongated and their nuclei flattened. They become very numerous among the tubules, and appear to replace the connective tissue cells in the cortex. By proliferation and anastomosis they gradually form the complex network which is found in the fully developed kidney.

The origin of the Mesoblastic envelope has already been mentioned, there are two main views.

I. Peritoneal Epithelium. Braun after examining the development in Lacertilia arrived at the conclusion that the tissue, out of which the tubules of the Metanephros were formed, was derived from irregular solid ingrowths of Peritoneal epithelium. "Peritoneal Zellstränge."

II. The Intermediate Cell Mass. This was the view enunciated by Sedgwick (Bb 76.) in the development of the chick. Sedgwick believed Braun's view to be erroneous. He showed that in the chick part of the Intermediate cell mass was at first continuous with the peritoneal epithelium,and had a continuation of the body cavity into it, but subsequently it became detached,and lay between the peritoneum and protovertebrae,and formed the Wolffian blastema. Sedgwick allowed that part of the blastema was formed from peritoneal epithelium, not as solid ingrowths in the way described by Braun, but as a continual process of budding of cells, which travelled inwards and united with the cells of the blastema. From the Wolffian blastema thus formed, Sedgwick believed the tubules of the Wolffian body arose as far back as the 30th segment.

But the blastema from the 30th to 34th segment in the chick remained for a long time passive, and was called by Sedgwick the kidney blastema. It is from this that he believed the tubules of the permanent kidney arose. With the appearance of the ureter the kidney blastema altered its position further from the peritoneum, so as to lie to the inner side of the ureter. After a time it broke away from the Wolffian body, and invested the anterior end of the ureter, collecting especially round the dilatations.

From the cellular investment, tubules and Malpighian bodies were formed in connection with branches of the ureter. The manner in which this came about was only imperfectly described.

Wolffian tubules and kidney tubules have a similar origin then according to Sedgwick. Schäfer takes the same view as regards the development of the human kidney, and it seems probable that the history of development is much the same in all the higher Vertebrates. The views of Braun and Sedgwick are not really very different, and we must regard the envelope of the ureter branches as composed of mesoblastic cells developed from the Intermediate cell mass and peritoneal epithelium. The envelope produces Malpighian bodies, tubules, connective tissue, and blood vessels, and forms a layer at the periphery of the ureter branches, which may be compared to the periosteum surrounding bone. Unlike periosteum its functions cease at an early date, the portions of the interlobular septa which lie nearest the pelvis disappear first, the layer under the capsule persists the longest, but no more tubules are formed after the 8th month or early part of the 9th. In connection with the tubules last developed Malpighian bodies form, but do not reach full development till the time of normal birth, and in some cases later. The Subcapsular layer gives rise to the ordinary kidney cortex, while the interlobular septa form the inter-pyramidal cortex. As mentioned above the process ceases in the latter, while it is still going on under the capsule. The oldest Malpighian bodies in the kidney are those which lie nearest the apex of the papilla in each lobule, the more recently formed are further from it, and the last are developed under the capsule, but as will be shown later never next the capsule, a zone containing convoluted tubules being interposed between them and the capsule.

Let us now return to the Cap or Cell mantle which forms in the kidney "Anlage." A mass of cells has been shown to develope in relation to the peripheral end of a collecting tube as in Fig. (4.). The Ampulla continues to grow, not as a solid mass of cells but as a hollow tube, the cells under the capsule proliferate at the same time. Meanwhile the cap extends and is found reaching down some distance on either side of the collecting tube. The cap begins to thin over the extremity and the two sides become detached. Fig. (4.) shows the thinning in the centre of the cap. The Ampulla then begins to divide into two branches, each of which remains in close association with one of the divisions of the cap. Fig. (5.) shows a still later stage. The end of the collecting tubule is cut obliquely, and does not show the dichotomous budding of th of the Ampulla. Over its end is forming another cap, and to one side is seen one of the divisions of the first cap. Owing to the elongation of the collecting tubule this division is now no longer immediately under the capsule, but lies deeper in the cortex. While this alteration in their relative positions is going on through elongation and division of the collecting tube, the cells composing the cap alter in shape and appearance.

The cells become greatly elongated, and narrow, and their nuclei large, and deeply staining. In this they offer a contrast to the cells of the collecting tubule, which are more cubical, and stain less deeply. The cells become arranged with their long axes radiating out from the centre in which a lumen appears. Fig. (5) shows the character of this hollow vesicle, the "vesicule rènale" of Èmery. It is composed of long thin columnar cells with central lumen, and is sharply defined from the surrounding connective tissue, and close to, but also separated from, the collecting tubule. By active proliferation of cells the vesicle grows in length, but not as a straight tube, it becomes comma shaped as in the next Fig. (6.). The bend of the comma is always away from the collecting tubule with which it eventually joins . Here we see one of the divisions of the Ampulla, which now curves a little under the capsule, but never completely round in the way described by Ribbert. Over its end is another cap forming, and just under its extremity is the comma shaped body. The cells now are even more cylindrical than before, and form a single layer. The tail of the comma is directed away from the collecting tube. In it a differentiation of cells is already taking place, the ones forming the convex bend of the tail are less cylindrical than the others, it is this portion that forms part of Bowman's Capsule, and these cells constitute its earliest lining. The comma is now in close contact with the Ampulla, but the lumens are not continuous. As the comma shaped body grows it elongates, but the tail remains in the same position, further growth is upwards towards the capsule along with the end of the collecting tube. It grows more quickly than the latter, and takes on another curve at its upper end, this time towards the Ampulla. The result is an S shaped body with a central lumen. Fig. (7). When the S is well developed its lumen becomes continuous with the lumen of the collecting tube. Fig. (10). The S shaped tubule is well known since Golgi's description of it, but Golgi considered it to be a structure continuous with the collecting tubule from the very first. One can often find the two in continuation as in Golgi's diagram, but these are late stages. They are well shown in Figs. (10 + 11.)

The two structures are intimately associated, but are not in continuity from the beginning. Golgi showed that the lowermost limb of the S surrounds the glomerulus, and forms the Malpighian body, the middle one developes into the proximal convoluted tube and Henle's loop, while the upper limb forms the distal convoluted tube and the junctional tube. Figs. (11&13) show that this is the case, and being photo-micrographs of actual sections demonstrate it in a way no diagram could.

The origin of the Malpighian bodies cannot then be considered by themselves alone, they are part of a structure which forms several of the most important parts of the kidney. Their origin is a complex one, and involves at the same time the origin of convoluted tubules, and connective tissue, and their further development is closely associated with the growth of the entire organ.

There has been even more difference of opinion on the origin and development of the Malpighian bodies than on the origin and development of the convoluted tubules. In the first place there have been two opposite views.

I. That the Malpighian bodies were formed at the peripheral ends of ureter branches, and that their epithelium was developed by proliferation of cells, which originally sprung from the Wolffian duct by way of the ureter. This was the view of Remak, Waldeyer, Toldt, Kölliker, Lieberkühn, Pye, Ribbert, Hortolès, Golgi, Nagel, and Berry Haycraft.

11. That the Malpighian bodies arose in the kidney cortex independent of the Ureter branches, and united with them secondarily. Their epithelium was not developed from the Wolffian duct, but from masses of mesoblastic cells which surrounded the anterior end of the ureter. With this view agreed Thayssen, Riedel, Kupffer, Bornhaupt, Braun, Fürbringer, Balfour, Sedgwick, Èmery, Hamburger, and Schäfer.

My own observations as already indicated lead me to believe that the second view is the correct one.

Colberg (Bb 13.) described two systems of tubules, one forming the looped canals and developing from the periphery, the other the ureter branches and growing from the pelvis. He further believed that Malpighian bodies developed in both systems, some being formed in connection with the loop forming canals, and others at the end of the ureter branches. This description is incorrect, Malpighian bodies certainly develope after the tubules have become continuous; but the part of the tubule they develope in is not an outgrowth from the ureter.

Löwe (Bb 57.) believed that the epithelium of the Malpighian bodies was derived from the Ureter branches, and that the mesoblastic cells formed the vascular part of the glomerulus. With this I cannot agree. The vessels are certainly formed from mesoblast, but do not play the active part they are generally credited with.

The mode of formation of Malpighian bodies has also been very differently described. They have been regarded as made up of two structures, Vascular and epithelial, each of which has been considered by different observers to take an active or passive part.

Remak (Bb 64.) in 1855 was the first to describe the formation of the Malpighian bodies. He believed that the end of a column of cells surrounded a glomerular tuft, and by degrees enclosed it. The epithelium played the active part at first, but by the further growth of the capillaries a basin shaped invagination of the tube came about. The cells lining the end of the tube were cylindrical, but gradually became flattened, the tuft pressing inwards so as to narrow but not quite obliterate the lumen. Remak said the process took place either at the end, or in the side wall near the end of the tubule. The value of his description lay in the fact that he established the presence of a layer of cells over the glomerular tuft.

Toldt (Bb 84.) confirmed Remak's observations and described the process more fully. He stated that the tubules ended blindly in spherical dilataions, and that in their further development capillaries appeared, which pushed in one side of the wall gradually invaginating it. He compared the process to the driving in of one side of a hollow india rubber ball till the two sides came into contact. This description has been followed in some modern text books, it is delightfully simple and wholly inaccurate.

Kölliker was of the same opinion as Toldt, that the wall of a tubule was invaginated by blood vessels.

Bornhaupt (Bb 5.) described the Malpighian bodies as arising from solid spherical masses of cells in the cortex, which became hollow and by a thickening of their wall at one side formed a glomerulus, and gradually assumed their later appearance. Bornhaupt believed the epithelial portion to be chiefly concerned in their development, and the glomerulus was formed, not by an ingrowth of capillaries, but by a thickening of the epithelium in that part of the wall which became the glomerulus.

Thayssen (Bb 83.) stated that the Malpighian body arose from a solid clump of cells in which a split like lumen appeared, but he did not describe it any further.

Riedel (Bb 67.) showed that solid masses of cells in the cortex became hollow, and gradually formed Malpighian bodies. He compared each corpuscle to a deeply hollowed spoon, of which the handle formed the tubule, and the hollow contained the glomerulus, while the convex back of the spoon represented Bowman's capsule.

Previous to the last three observers Colberg (Bb 13.) had described the development of Glomeruli in the kidney. He injected the blood vessels and found that some of the Glomeruli showed the injection, but others did not. He described the urinary tubes as ending in the cortex partly as club-shaped swollen ends, partly as betufted ends, and partly as injected Glomeruli. The non-injected ones he called "Pseudo-glomeruli", though what he meant by that term is not quite clear. Hamburger (Bb 29.) interprets it as meaning that Colberg did not recognise their nature, but the assumption is not quite warranted from Colberg's description. The name "Pseudo-glomeruli" given by Colberg to certain structures in the cortex of the kidney has been retained probably on account of so little being known about them. The name was clearly given to Malpighian bodies in an early stage of development and need not be retained. It is useless and misleading.

Pye (Bb 61.) expressed views very similar to those of Remak's. He stated that the end of a tubule curved round the glomerulus so as to embrace it and become its capsule.

Ribbert (Bb 65.) described it similarly. He compared each urinary tubule to a man's arm, the end of the tubule being represented by the hand. The tubule curved round in a way represented by flexion of the wrist and fingers. The hand with fingers flexed on the palm represented the early stage of a Malpighian body, the skin of the dorsal aspect of the hand being equivalent to Bowman's capsule, and the skin of the palmar aspect to the covering of the glomerulus. Capillaries grew into the space between fingers and palm, which was at first wide, but gradually closed to form the neck of the glomerulus.

All the foregoing observers described the flattening of the epithelium lining Bowman's capsule and covering the glomerulus. Schweigger Seidel (Bb 75.) in addition pointed out that there was a great difference for some time between the kinds of cells in the two places. The cells covering the tuft remained cylindrical for a considerable period of time after the cells of Bowman's capsule had become flattened. Ribbert recognised this when he described the

Malpighian body as a sickle shaped structure with two different layers of cells uniting at the end of the sickle. The cells of the outer layer were flat, those of the inner cubical, and opposite the middle of the sickle cylindrical, a split like lumen appearing between the two layers. Hortolès (Bb 37.) admitted a cellular covering to the glomerulus during development, but believed that the cells fused together later to form one endothelial cell with multiple nuclei. This is very unlikely.

Nagel (Bb 57) in 1889 described each urinary tubule as ending somewhat widened, with its epithelium passing over a prominence of connective tissue, which became the glomerulus by formation in it of capillaries. The cells which became the lining of Bowman's membrane were flat at an early stage, while the cells over the glomerulus were cylindrical, and resembled those of the convoluted tubule.

Nagel agreed with Toldt that the capillaries were the active agents in the formation of the Malpighian bodies.

Hamburger (Bb 29.) in 1890 found that the Malpighian bodies arose in the manner described by Bornhaupt and Riedel. A shell like structure was formed with its concavity towards the capsule of the kidney, consisting of two layers of cells, an inner and an outer separated by a split like lumen. The cells of the inner layer were cylindrical, those of the parietal layer were flat. The inner layer covered the glomerulus, the outer formed the lining of Bowman's capsule.

None of the foregoing observers have described the development of the Malpighian body fully, nor do their descriptions all agree. The process described by Remak and Toldt differs very considerably from that described by Bornhaupt and Riedel. As far as I am aware none of their papers have been illustrated by photographs of actual specimens, and the diagrams employed instead cannot but be misleading when one wishes to enquire into detail, such as the character and shape of the epithelial cells in different situations. The photographs illustrating this part of the paper are taken from sections of Human kidneys of from 4 to 6 months old.

Mode of Formation of the Malpighian Bodies.

The origin of the Malpighian bodies from the mesoblastic envelope of the kidney has already been described. There are usually two developing simultaneously, one on either side of the extremity of each collecting tube. The cells from which they are formed are at first situated as a Cap on the end of the Ampulla, and are therefore to be found immediately under the capsule, or in an interlobular septum; but with the further growth and bifurcation of the end of the collecting tube, the Cap divides, and each half is pushed aside. The cells meanwhile go on proliferating, and form a group on either side of the collecting tube now some distance from the capsule. The cells are irregularly arranged in several layers at first, Fig. (4.), but gradually elongate with their long axes radiating outwards, and a lumen appears in their centre. Fig. (5.). A tendency to spiral arrangement soon shows itself, and the end of the vesicle nearest the medulla grows outwards away from the collecting tube. In this way a "Comma" shaped body is formed, the lumen being continued into the tail, which is always directed away from the collecting tubule, and ends in a fine point always turned towards the periphery of the lobule.

The cells lining the vesicle are cylindrical and narrow, with long deeply staining nuclei; compared with the cells of the Ampulla they are longer, more irregular, and their nuclei take on a much deeper stain. Fig. (5). With the formation of the Comma shaped body the cells begin to differentiate; in the part next the Ampulla they go on elongating, but in the tail there is a marked contrast between the cells on either side of the lumen. On the concave side, which is the side towards the periphery of the lobule, the cells become elongated, their nuclei large, and even more darkly staining; on the convex side, the cells are smaller and more cubical, while towards the point they appear drawn out so that their long axes are almost parallel to the lumen. Fig. (6-8).

The tail of the Comma shaped structure is the beginning of a Malpighian body. The concave side with the elongated cells is the first appearance of the glomerulus; the convex side becomes the outer layer of Bowman's capsule, and the lumen is the cavity of the Malpighian body.

It is this early stage of the Malpighian body that has been known as a "Pseudo-glomerulus" Fig. (9-11). Riedel's comparison of it to a deeply hollowed spoon is a very suitable one, the developing glomerulus occupies the hollow, and Bowman's capsule is represented by the convex back of the spoon.

The remaining portion of the Comma developes into the convoluted tubules and Henlès loop. The lumen of the tube is continuous with the cavity of the Malpighian body from the very first, and the tube does not begin opposite the glomerulus as in the adult, but to one side of its base. The first appearance of the cavity of Bowman's capsule is a narrow slit, and never a vesicle in the Human Kidney. Toldt's description of the driving in of one wall by capillaries is not an accurate one. At this stage there are no capillaries in the glomerulus. The glomerulus appears rather to be as Bornhaupt described, a thickening of the cells on one side.

The Malpighian bodies during development have always the same relation to their surroundings at each stage. The glomerulus always developes on the side of the lumen next the periphery of the lobule, and Bowman's capsule is to the medulla side. The origin of the tubule is always to the side of the cavity next the collecting tube with which it eventually joins, and consequently the tubule leaves the Malpighian body close to the base of the glomerulus, and is always directed outwards towards the periphery of the lobule, e.g. towards the capsule or interlobular septum, and is parallel in the first part of its course to the collecting tube. These relative positions are maintained for a long time, and I have never seen an exception. The photomicrographs have all been arranged so that the capsule of the kidney is above and parallel to the upper margin of the plate. It will be noticed that in all the glomerulus hangs downwards, and this is always the arrangement in the foetal kidney, every glomerulus has its base towards the periphery of the lobule. The Malpighian bodies seem to be fixed structures at an early period, and do not move their position as do the tubules during further growth. This is an important fact, and is not explained altogether by the vascular arrangements. The early fixation seems to be due to the density of connective tissue round the Malpighian body, and it is likely that a certain part of it always remains constituting the frame work. The convoluted tubules and Henle's loop especially appear to be free, and alter their relative positions enormously during growth, but the extremity, the Malpighian body, remains fixed throughout life, and is so from its first appearance.

A noticeable feature about the early Malpighian body is the large size of its cavity, this is probably due to contraction of the part which forms the glomerulus. With the further development the cells lining the two sides become more and more different in character. Those which form the Glomerulus proliferate rapidly, and are large and cylindrical with deeply staining nuclei. Instead of being one layer deep they are usually several. Fig. (8.). The cells on the opposite side of the lumen, which form the cells lining Bowman's capsule, are fewer in number, and are spread out instead of being closely packed together. They gradually become flattened, and this flattening takes place very early; by the time the tubule joins with the collecting tubule, they have become quite flat, and can scarcely be distinguished from the cells of the surrounding connective tissue. This is shown in Figs. (20 - 22.) which are cross sections, and not parallel to the line of the tubule, and are more highly magnified. In the other Figs. (7 to 12.) the process can be traced, the cells which are first altered are those at the far extremity from the tubule, as a rule there is a gradual transition from that point to the cylindrical cells of the tubule. At the far extremity the transition is sudden where Bowman's capsule becomes continuous with the glomerulus, the flat cells in single layer become cylindrical as soon as they turn the point. On the tubule side of the glomerulus the cells also flatten a little, but not as markedly , they mark the position of the neck of the Malpighian body. At this stage the neck is represented by a fairly wide lumen, and is lined by cubical cells which rapidly become cylindrical as they pass into the tubule, while on the capsule side of the neck they differ on either side of the lumen, those forming the glomerulus again becoming cylindrical as described, and those lining Bowman's capsule gradually flattening till they resemble endothelium.

The Glomerulus.

The Glomerulus is at first formed by a thickening of cells in the position indicated, and is not vascular. If the surrounding connective tissue be carefully examined no capillaries can be seen, but there are some connective tissue cells close to the base of the glomerulus. When the S shaped tubule is formed, the space between the lower and middle limbs is occupied by these cells, they are few in number, and resemble the other cells which are found in the Matrix of the cortex. From these cells I believe the capillaries of the glomerulus are formed in situ, and not as ingrowths. Capillaries and the cellular covering develope together, and are joined by a branch from the renal artery at an early period, but the connection is not established until the lumens of collecting and convoluted tubules have become continuous. The cells covering the glomerulus go on proliferating, and form a basin shaped swelling, in the hollow of which the capillaries develope. The cells are cylindrical with large nuclei, and little protoplasm, and take on a very deep stain. Figs. (20 to 22.) show this very well. The further growth in size of the glomerulus may be described as an invagination, but it is not an invagination of the kind usually supposed. None of it takes place at the expense of the other side as occurs in Toldt's illustration of the India Rubber ball. It is rather an increase in size by proliferation of its own constituents; the base remains in the same position, and is wide at first, but gradually narrows, the narrowing being brought about by the formative action of the large cells in the covering. In a simple invagination, as of one side of an India Rubber ball, the base becomes larger as more of the wall is pushed in. The cells covering the glomerulus seem to have a special function in shaping it , and they afterwards grow into its interior and split it into lobules. The character of these large cells is well shown in Fig. (22.), a high power view of a glomerulus in which capillaries have begun to form. A single layer of almost cylindrical cells with large nuclei cover the glomerulus, and at intervals there are seen similar cells dipping into the interior. In Fig. (21.) these cells are further in, and have divided the glomerulus partially into lobules. The contrast between these cells and those lining Bowman's capsule is very marked at this stage.

The cells contained in the interior of the glomerulus Fig. (22) also proliferate, their nuclei are smaller and rounder than those of the cells covering them. Spaces are soon formed which are the lumens of capillaries, and with the increase in size of the tuft these multiply, and are arranged into lobules by the ingrowth of the surrounding cells. The cells forming the capillaries elongate, and their nuclei flatten and become less evident. After the glomerulus has been divided into lobules, and the capillaries have assumed their shape, the cells of the membrane covering them also flatten, Fig. (23.), their nuclei grow smaller, and they gradually take the appearance characteristic of the fully developed glomerulus.

The cells of the membrane covering the glomerulus take the important part in its development. They are responsible for its first appearance, and afterwards regulate its shape, and divide it into lobules. It is not till the glomerulus has been fully formed, and the capillaries definitely arranged, that the cells of the membrane lose their shape, and flatten out. It would seem that this part of their function over, they have a tendency to behave in the same manner as the cells lining Bowman's capsule. Both have been shown to arise from the same cell mass, and to resemble one another at first. They are mesoblastic structures, but assume the character of epithelium; the cells lining Bowman's capsule apparently having no further function than to form the lining of a space rapidly reassume the characters of the mesoblastic cells which line other body cavities; the cells covering the glomerulus have a further function to perform and develope accordingly, but when the glomerulus is fully formed, they also assume the shape of endothelial cells. Owing to their position the cells covering the glomerular capillaries must have some function, and no doubt they are modified accordingly. Whether they play an active or a passive part in urinary secretion is not yet determined.

The presence of connective tissue in the glomerulus at an early period is quite evident, and from the mode of development it is not impossible that some remains when the Malpighian body is fully formed. Its place seems to be taken by capillaries, but there is no reason why some cells should not remain. There may also be nerves and lymphatics. Certain it is that in some adult kidneys spaces may be found in the glomerulus which are not capillaries. Professor Greenfield has pointed them out to me, they may be lymphatics but it is a difficult matter to prove them to be such. The presence of lymphatic rootlets in the kidney has usually been taken for granted since Ludwig and Zawarykins' researches (Bb 53.), but when one studies the methods employed, and the results obtained by these and other observers, one is inclined to doubt the value of their observations. Any method of injection by employing pressure is bound to be fallacious, artificial spaces are readily produced, and rupture into the capillaries may also occur. The injection of fine particles into the kidney of living animals might give more reliable results. My own observations have been of negative value.

The neck of Bowman's capsule.

In the adult kidney the neck of the tubule is usually opposite the base of the glomerulus. In the Malpighian body undergoing development the tubule always leaves the cavity next the base of the glomerulus, and to that side of it which is towards the collecting tube. The process of alteration from this to its position in the adult I have not seen described, but it is very well shown in the Figs. (13-19). At first the cells covering the glomerulus are continuous in an unbroken curve from the glomerulus into the convoluted tube, Figs. (11-12), and the lumen is wide. The cells at the future neck however soon begin to thin and become cubical in shape, while the lumen narrows. Fig. (12.) shows a condition which is not quite so common, the neck is very long and has a wide lumen; the greater part of it afterwards becomes convoluted tubule. An indentation usually appears at the base of the glomerulus at the same level as the apex of the lumen on its other side. Fig. (13.). In the next Fig. (14.) a further stage is shown, there is now a definite recess between the base of the glomerulus and the origin of the tubule. The succeeding Figs. (16 to 19.) show the further development of this recess. It is lined internally from the very first by flat cells similar to those of Bowman's capsule already formed.

The wall between this, the later developed portion of Bowman's capsule is well seen in Fig. (17.) to consist of the wall of the first part of the convoluted tubule. This arrangement persists for a long time. At the apex of the dividing wall where the cavity of the capsule becomes continuous with the lumen of the tube, there is always a sudden transition between the characters of the cells; those lining the capsule are flat, those lining the tubules are cubical. On the other side of the lumen there is not this sudden transition, but the cubical cells in the neck become less cubical as they pass over the capsule until they are opposite the middle of the glomerulus, when they become flat. Bowman's capsule contains cubical cells for a considerable time, and they are always in this situation, e.g., the half of the capsule that is on the side of the origin of the tube. When the Malpighian body is fully developed, these cells form part of the convoluted tube. It follows therefore that part of what seems to be originally Bowman's capsule is not so in the fully formed Malpighian body. Nearly one half of Bowman's capsule is a later formation, and grows outwards from the base of the glomerulus, until the neck of the tubule is in a position opposite the entrance of the vessels. That this is the mode of formation is easily seen, it is not a rotation of the glomerulus. The base of the glomerulus is fixed, and remains in the same position relative to the collecting tubes and periphery of the lobule. The tubule at first leaves the capsule nearest the periphery of the lobule, but eventually comes to leave it at the furthest point from the periphery. Part of the process comes about by the gradual constriction of the base of the glomerulus, the cavity extending inwards, but I believe that the immense and rapid growth of the convoluted tube is the chief factor. The tube by its growth descends towards the medulla, and carries with it the neck, until that has reached the lowest point it can get to. The process can be easily followed in the plates.

The neck of Bowman's capsule then varies in position during development, its lumen is at first wide but when fully developed is slightly constricted. Cubical cells are found continuous from the tubule into the capsule at the side of the lumen opposite the glomerulus, but they do not extend as a rule beyond a point opposite the entrance of the vessels. In the fully developed Malpighian body the cubical cells are not as a rule continued beyond the neck, Bowman's capsule being lined by the flattened cells alone. Exceptions to this rule are found. In some Mammalia, e.g. the mouse, the cubical cells often line a third or even more of the capsule.

Bowman's Capsule.

This has been for the most part described already, but some points in its formation need emphasis. It has been shown to consist of two parts, one of which is formed considerably later than the other. Bowman originally described the capsule as consisting of a basement membrane lined with cells. In the developing kidney the cells alone appear to constitute the wall of the capsule, the basement membrane is a later formation still. The cells arise in common with the origin of the rest of the Malpighian body from the mesoblastic kidney envelope. They become elongated and are situated in the tail of the comma shaped body opposite the cells that form the glomerulus, a split like lumen separating them. Though almost cylindrical at first, they rapidly become cubical, and at the extremity of the lumen are quite flat at a very early stage, forming a single layer. Fig. (8.). At the middle of the capsule opposite the base of the glomerulus, they gradually become more and more cubical till they join the cells of the convoluted tubule. The greater part of the capsule becomes convoluted tubule at a later stage, the septum being formed by the downward growth of the tube in the manner already described. The cells lining the later portion of the capsule are flat from the very first, and apparently grow by proliferation of the existing cells, which line the capsule around the base of the glomerulus. In every section of foetal kidney one finds numbers of Malpighian bodies where the cells lining Bowman's capsule are cubical, and it is easily seen how this comes about. The section has passed through that part which forms the capsule for the time, but which is not really true capsule as found in the fully developed Malpighian body. Fig. (23.) shows this, the cells lining Bowman's capsule are here close to the neck of the tubule.

Though no basement membrane can be distinguished outside the cells, there are often several layers of cells of similar character closely applied to them. Figs. (20-22) show them. The cells are long and flat, with thin drawn out, and deeply staining nuclei arranged parallel to one another. All bear a striking resemblance to endothelial cells. They might be regarded as going to form the basement membrane if we accept Ludwig's view that the basement membrane is a mosaic of flattened cells, and Roth's that it is composed of endothelium. The homogenous membrane met with in the adult kidney is absent. How it is formed, and what it is composed of, is still unsettled.

It is probable that from the mesoblastic origin of Bowman's capsule the cells may be regarded as endothelial, and the space contained by them as a small body cavity, specially adapted for excretory purposes. This view is supported by the history of the Malpighian body in comparative Embryology. Its origin also in Man from the Intermediate Cell mass and Peritoneal epithelium, if Sedgwick's description is right, is an additional fact in favour of this view.

The Origin of the Convoluted Tubes.

The Convoluted tubes arise in the manner already described, in common with the Malpighian bodies, from solid cell masses in the Mesoblastic covering of the Ureter branches. The cells become cylindrical, and arrange themselves round a central lumen, forming the body of the Comma. Their subsequent development is shown in the Figs.(7 & 13.). In place of a vesicle a tubule is formed by its elongation, which takes on a curve in its upper part towards the Ampulla. The lumen of the tubule is now S shaped, the upper and middle limbs of the S being the parts from which the convoluted tubes develope. The cells which line them are at first cylindrical with long and deeply staining nuclei, and offer a great contrast to the cells of the collecting tubule. Fig. (7.). There often seems to be several layers of cells at first, but eventually there is only one. The lumen is narrow, but widens out considerably at the lower bend of the S, where tube joins Malpighian body. The S is closely applied to the under surface of the Ampulla, but their lumens are not continuous at this stage. With further growth a thin process from the under side of the Ampulla unites with the thinned extremity of the upper limb, and the two structures become continuous, a narrow lumen forming between them.

Fig. (10.) shows the thin portion of tubule connecting them, the section here passing through its widest part. The cells of the narrow connecting tube are small, and their lumen joins the Ampulla at right angles to the collecting tube. It is this small tube which connects the two independently developed structures that is known in the fully formed kidney as the Junctional tubule. Here the tubules of the Kidney blastema unite with the extremities of the ureter branches, and Mesoblast joins Epiblast, if we are to regard the Wolffian duct as Epiblastic.

It is seen that the tubule which forms the convoluted tubes is very early divided into two limbs, the upper two of the S. This distinction is maintained and increased. The cells which form them multiply very rapidly, and form a single layer with central lumen. Owing to the rapid increase in length of the tubule, the convolutions become greater, the middle bend, or rather the one which is between the two upper limbs soon shows a tendency to growth downwards towards the medulla. Figs. (9 & 13) illustrate this. In Fig. (12.) the bend has reached to the level of the Malpighian body, and it continues to descend parallel to the collecting tube. It is this bend which afterwards constitutes Henle's Loop, and the parts of the tubule on either side of the bend formed the ascending and the descending limbs of the loop. The limbs of Henle's loop pursue a parallel course, and are straight. They gradually descend during further development, and eventually reach the peripheral part of the medulla. The cells lining them also flatten, but not to such an extent as the cells lining Bowman's capsule.

The portion of the tubule between Henle's loop and the Malpighian body forms the proximal convoluted tubule; the portion beyond Henle's loop, and between it and the junctional tubule, becomes the distal convoluted tubule.

From their mode of development it is clearly seen that, as Golgi described, both proximal and distal convoluted tubes closely surround the Malpighian body with which they are associated; and further, that the limbs of Henle's loop in their upper part are also in close proximity to the Malpighian body. One often sees in a section one narrow tubule, and sometimes two, in close relation to the base of the glomerulus. Fig. (19.). These are the limbs of Henle's loop belonging to it.

The convoluted tubules go on growing in length, and as they are not fixed in the way the Malpighian body is, they form many convolutions in the cortex. As already shown it is by this increase in length that the neck of the tubule comes to occupy a position opposite the base of the glomerulus.

During their growth the cells undergo a change in character, they are larger and broader; Fig. (19.) The nucleus is relatively smaller, round, and more deeply placed in the cell. The protoplasm is large in amount, and granular, and stains well with rubin and orange. I have not seen the rodded character described by Heidenhain.

The Ampulla.

The Ampulla is a structure of great importance. It is always to be found in the periphery of the lobule, either under the capsule, or the interlobular septa. It is therefore in the formative area, where everything is in active growth. The Ampulla like its surroundings is constantly growing, but not in the way described by Toldt. My own observations lead me to believe that it does not send out solid branches, but hollow buds. Each Ampulla is the dilated end of a collecting tube, and forms the extremity of one ureter branch. It is lined by a single layer of cells, and has a large lumen. Fig. (7.). Growth occurs at the peripheral end, and in this way the straight character of the collecting tube is produced. After division of the cap of cells over it, the Ampulla usually begins to bifurcate, two hollow buds being gradually pushed out from the extremity. Each bud enlarges and forms a new Ampulla, with which the S shaped tube joins on that side. The two branches separate from one another, and each bends to a certain amount under the capsule or septum. Fig. (8.) shows this bending, which in this instance has reached what appears to be the furthest extent usual.

After junction has been established between it and the convoluted tubules, the Ampulla still goes on growing. Figs. (9 - 10.). A new cap of cell appears above it, and the process is repeated. After the 8th month the growth of the Ampulla ceases, and in the interlobular septa it appears to cease before that time. The last Ampulla formed merely unites with the convoluted tubule, and a simple bend under the capsule results.

In this way every collecting tube branches, and is joined by convoluted tubules, the oldest being the nearest to the medulla, and the latest at the periphery of the lobule.

In every section of developing kidney there are therefore Malpighian bodies and tubules at different stages. The oldest are fully formed, and lie deepest in the cortex. A narrow zone at the periphery of the lobule is the formative area, in which Malpighian bodies, convoluted tubules, junctional tubules, and Ampullae are gradually produced, and all except the Ampullae are left behind to perfect their structure from the material which has been constructed there.

Connective Tissue.

Connective tissue is large in amount in the foetal kidney, but diminishes with the growth of the glandular element, and by the time of normal birth there is remarkably little left. In the cortex of the developing kidney the matrix is very abundant and cellular, in the deeper parts the cells become myxomatous, and their place is eventually taken by the tubules, and blood vessels. Each primitive cone is surrounded by connective tissue, and may be said to occupy a special compartment. The septa between the compartments are well marked, and cellular, not fibrous; there is in fact a framework, which may be compared to Glisson's capsule in the liver. It does not appear to develope further, and is greatly thinned owing to the great increase in size of the compartments by the enormous growth of the convoluted tubules. It is probable that vestiges of the septa persist, and form the fibro-cellular framework described by Goodsir. More connective tissue is found in some places than in others. In the Papillary region there is a considerable amount between the collecting tubes, and this is easily explained. The collecting tubes do not increase the breadth of the papilla by forming convolutions, they are developed early, and always remain separated by connective tissue, the septa are not expanded and thinned, as they are in the cortex. The great increase in breadth of the pyramids comes about by the descent of Henle's loop between the collecting tubes, but as Henle's loops do not descend to the apex there are left below them wedge-shaped spaces between the large tubules or Ducts of Bellini, in which the connective tissue persists.

There always remains a certain amount too round the Malpighian bodies, and especially at the bases of the glomeruli. It helps to keep them fixed structures, a provision which is rendered necessary by the enormous growth in length of the convoluted tubules.

Connective tissue is also found under the capsule, and round the branches of the renal artery.

Blood vessels of the Kidney.

The development of the larger branches I have not studied. It seems probable that the branches of the Renal Artery lie at first between the first branches of the ureter, i.e. the branches which go to form the pyramids, and the mesoblastic envelope. From these arteries vessels are given off at right angles which follow the collecting tubules in their peripheral growth. Though called Interlobular Arteries they are not strictly interlobular, but each lies in a septum between two adjacents primitive cones, and gives off single branches, the afferent-arterioles to the glomeruli of those cones. The interlobular arteries give off as many branches as there are origins of tubules in the cortex, and it is very probable that they do not exceed this number, Ludwig (Bb 52.).

The capillaries of the glomerulus seem to form in situ from mesoblastic cells which are embraced by the lower limb of the S shaped tubule.

The capillaries of the network round the convoluted tubes continue developing by branching and anastomosis as the tubes increase in length and complexity.

Mode of Growth of the Kidney.

The individual structures which make up the kidney have already been studied separately, but it is necessary to consider them as a whole.

Malpighian bodies begin to form at the end of the second month, and new ones are continually being added up to the end of the 8th, or beginning of the 9th month.

The collecting tubes on the other hand are formed early, a certain number of branches are given off and these multiply by frequent branching towards the cortex. There is no evidence that new tubes grow out from the pelvis.

The branches of the ureter which correspond to the papillae each form a lobule by repeated branching. The lobules are almost completely separated from one-another by the mesoblastic envelope, which forms a double septum. After the 7th month the cells constituting the septa begin to disappear, from the pelvis outwards, and in the 9th month scarcely any of the mesoblastic envelope is left.

In all sections of foetal kidney one notices the much larger number of Malpighian bodies relative to the adult kidney. Convoluted tubules which make up the greater part of the cortex in the adult are almost absent at the 4th month. Fig. (/.). At the time of birth there are as many Malpighian bodies in the kidney as there will ever be. Some of these are certainly not fully developed, and occasionally one finds imperfectly formed ones some time after birth, but no new ones develope. At birth all the structures in the kidney are already formed, and further growth is but a finishing and enlargement of existing structures.

This has been recognised for some time, and Schweigger Seidel (Bb 75) has divided the growth of the kidney into two periods. "An Embryonal", and a "Post Embryonal". In the first period growth takes place in two ways. One by an Apposition or formation of new material in the periphery. The other by increase in size of material already formed. In the Post embryonal, the formation of new material has ceased, and growth now takes place by an increase in size only.

Riedel found that the first periods did not always correspond to the period of Intra-uterine life. In mice and in other blind born animals the formative process continued for as long as 14 days, while in other animals the process ceased before birth.

During the first period the structures that lie the deepest increase in size, the Malpighian bodies become very large, some more so than they are in the adult kidney. The convoluted tubules increase in length and diameter. In the 4th month there is very little division between cortex and medulla.

During the second period growth of the cortex chiefly takes place by increase in the length and the convolutions of the convoluted tubes. Growth of the medulla comes about by increase in length of the collecting tubes, and by the descent of Henle's loops. As the result of these processes a definite arrangement of structures comes about. There is the broad division of kidney into cortex and medulla. Malpighian bodies and convoluted tubes are confined to the cortex, while the medulla is made of the distal ends of the collecting tubes and the limbs of Henle's loop. Part of the cortex is inter-pyramidal, and its mode of development has been described; these portions are also known as the Septula Renum or Columnae Bertini.

A Zone of the cortex, the subcapsular zone, contains ordinarily no Malpighian bodies, and the reason is evident, the convoluted tubes are developed peripherally to the Malpighian bodies, and some of their convolutions remain in that position. In the same way there is a deep zone in the cortex, where there are no Malpighian bodies, this may be explained by the manner in which the convoluted tubules tend to descend towards the papillae, so that the origin of the tube from Bowman's capsule is at the nearest point to the medulla, as a consequence there is always a certain amount of tube below the Malpighian body. These layers are not always perfect, one sometimes meets with Malpighian bodies next the capsule, but this is not the ordinary arrangement. In the same way though the base of every glomerulus originally is towards the periphery of the lobule, it does not always persist thus, and Malpighian bodies may be found which have rotated.

GENERAL CONCLUSIONS.

Origin of the Kidney.

The kidney has a double origin, each of which is quite distinct from the other, but the two come together at an early period, and remain intimately associated during further development.

1. The Kidney Blastema.

This consists of a mass of cells closely related to the Blastema of the Wolffian body, and apparently formed from the Intermediate Cell Mass, or the Peritoneal epithelium. It is therefore Mesoblastic. It forms an envelope round the ends of the Ureter branches, and persists as a thin cellular investment under the capsule, and between the lobules, until the end of the 8th month, after which it almost entirely disappears.

11. The Ureter.

This structure is an outgrowth from the Wolffian duct. It appears at the end of the 1st month, and grows forwards as a solid column of cells to reach and imbed its peripheral branches in the Kidney Blastema. It is not settled whether the Ureter is Mesoblastic or Epiblastic, but the balance of recent opinion is in favour of its being Epiblastic.

At the middle of the 2nd month the Ureter has come into apposition with the kidney Blastema, and the result is the beginning of the formation of a definite kidney.

The Ureter branches early, and its lumen dilates anteriorly to form the future pelvis and calyces. The primary branches are of a definite number, and at their extremities masses of cells appear constituting the "Nierenbecken" of the German writers. From these masses of Cells in the kidney pelvis, are developed the Collecting tubes of each lobule. From each cell mass, the tubules grow outwards in a radiating manner, and terminate in the Mesoblastic envelope immediately under the capsule. Ureter, pelvis, calyces, and collecting tubules, are therefore formed from the Wolffian duct, and these are the only parts of the kidney which are formed from the Wolffian duct, unless we include part of the Junctional tubule.

From the kidney Blastema arise the Malpighian bodies, convoluted tubules, Henle's loops, and the Junctional tubules, the connective tissue frame work, and capsule. Blood vessels appear to be partly of the same origin, and partly branches from the renal artery. The Blastema or "Nierenanlage" of the Germans forms a peripheral envelope from which the above structures are developed in succession. Owing to its surrounding the primary Ureter branches, part remains close to the pelvis between the lobules, where it constitutes double septa, which give rise to the Interpyramidal cortex. The septa disappear before the subcapsular layer, and no more glandular elements are formed after the end of the 8th month.

Malpighian bodies appear at the end of the 2nd month, together with tubules, which become the convoluted tubes belonging to them. They unite at an early stage with the Ureter branches, the point of junction always being situated at the periphery of the lobule.

Each Malpighian body and its tubule arise as a solid mass of cells at the periphery of a lobule, either under the capsule, or in the interlobular septa, in close relation to the dilated extremity of a Ureter branch or collecting tubule. The solid cell mass acquires a lumen, and takes on the shape of an S. The lower limb of the S becomes a Malpighian body, the upper and middle limbs form convoluted tubules, the bend between them constituting Henle's loop, while the extremity of the upper limb joins the collecting tubule, and forms the greater part of the junctional tubule. As a rule this process takes place on two sides of a collecting tube, the dilated extremity or Ampulla of which divides into two, each branch being joined by the junctional tubule of its side. The S shaped tubule has always the same relation to the collecting tubule, its long axis is parallel to, and its lower limb turned away from, the collecting tube.

Malpighian bodies.

The Malpighian body forms in the lower limb of the S shaped tubule, and is the first part to show differentiation. A split like lumen appears early, and attains considerable size. The convex side of the limb is formed by the epithelium which lines Bowman's capsule, the concave side by the epithelium which covers what becomes the glomerulus. The epithelium on both sides is similar at first, but only for a very short time, the cells lining the capsule thin- and become flattened, though not all over.

The Glomerulus is formed, not by an invagination, but by a thickening of the epithelium. The capillaries of the glomerulus develope in situ, and are covered by the epithelium. Further growth takes place by an enlargement of the capillaries, and proliferation of the cellular covering. Its shape is influenced by these cells, which are almost cylindrical in form, and arranged in s single layer. The division of the glomerulus into lobes comes about by the penetration of the epithelial cells between the capillary loops. When the glomerulus is fully formed the cells diminish in size, and become flattened, like the cells lining the true capsule.

Bowman's capsule is lined by cells which show a difference in two situations. From a point opposite the middle of the base of the glomerulus to the extremity of the capsule opposite the neck of the tubule the cells are long and flat from an early stage. The remainder of the capsule is lined by cells which become more and more cubical as they pass into the neck of the tubule, this part eventually becomes the first part of the convoluted tubule. It is completed by the development of a septum, which grows from the base of the glomerulus between it and the origin of the tube. The septum consists of a double layer of cells, that on the side next the glomerulus is of flattened epithelium, that on the convoluted tubule side is of large cubical cells. The neck of the tubule is at first wide, and situated close to the base of the glomerulus, but with the growth of the septum it passes to a point opposite the base of the glomerulus. Thus part of Bowman's capsule is a later formation than the other, and both are lined with flat cells. There is no basement membrane round the developing capsule.

The cavity of Bowman's capsule may be regarded as a body cavity specially differentiated for urinary excretion. Its lining consists of flattened cells, which are developed from cells closely allied to those which form the lining of the general peritoneal cavity; in Bowman's capsule they seem to have no further function than to form the wall of the cavity, and they assume at a very early period the character of the cells lining other body cavities; and this character is maintained under normal conditions throughout life. It is not therefore surprising that in certain inflammatory conditions these cells should proliferate, and form organised connective tissue. Professor Greenfield was quite justified in classing them as Endothelial from their pathological reactions; the history of their development lends additional support to his view.

The cells of the convoluted tubules attain a much higher stage of development, and once arrived at this stage it is doubtful how much retrogression can take place without dissolution of the cell. They are elaborated for the performance of special, and probably complex functions, and are more highly organised. Their reactions in disease are likely to be altered accordingly.

Malpighian bodies begin to form in the 2nd month, and continue appearing till the end of the 8th month. The new Malpighian bodies are always found at the periphery of each lobule.

Connective tissue exists in large amounts in the foetal kidney, but most disappears by the 9th month. It forms a septum between the primitive cones, and fixes the glomerulus in a definite position, but allows the tubules to elongate, and alter their relative positions.

Henle's loop is formed by the downward growth of the upper angle of the S shaped tubule.

Up to the end of the 8th month growth of the kidney takes place in a two fold manner, partly by apposition of new material in the periphery of the lobules, and partly by growth of already formed material. After the 8th month growth is due to increase in length of tubules, especially the convoluted tubules, no new Malpighian bodies or tubules are formed.

The arrangement of the different structures into the definite zones of the fully developed kidney is chiefly due to the arrangement of the connective tissue frame work, which allows the tubules to move freely in their growth, but holds the Malpighian bodies and large collecting tubes in fixed positions.

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A short sketch of the Comparative Anatomy

and Embryology of Malpighian bodies

with special reference to a few Types.

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The Comparative Anatomy of the Malpighian Bodies.

Malpighian bodies are peculiar to the excretory organs of the members of the great Phylum of "Craniata" Each Malpighian body contains a space into which projects a vascular tuft, the glomerulus, and from which a tubule leads to the exterior of the body. The wall of the space, known as Bowman's capsule in the more highly differentiated Malpighian bodies, is not always complete in the lower forms, but often includes several other structures, and allows access to the cavity from other cavities. In the highest forms however, Bowman's capsule completely shuts off the space from everything but the urinary tube which leads from it. Malpighian bodies therefore show a great variety in structure in the different Classes of the Phylum.

One would expect to find a gradual transition from the one to the other, the more primitive in the lowest types, and the more highly differentiated in the highest classes. But this does not exactly occur, there are missing links in the system, and the degree of development of the Malpighian bodies, does not always correspond to the degree of development of the organism as a whole. A more perfect series is found in Comparative embryology, and in some it would appear that their history of development is truly a recapitulation of the history of the race.

Definite excretory organs are found first in the Plathelminthes. In Taenia Solium, Distomum Hepaticum, and others of the flat worms, there exist a number of small tubes opening into larger canals, which open externally by pores. The fine branches end blindly, some of them in peculiar cells which have been called Flame cells, from the fact that they project one or more flame shaped cilia into the lumen of the tube. Parker (Bb 59.). There being no vascular system there cannot be anything of the nature of a glomerulus.

In Mollusca, Polyzoa, and Brachiopoda, the excretory organs are simple tubules often ciliated, and opening by one end into the general body cavity, and by the other on the exterior. These may be regarded as the simplest form of excretory apparatus.

In the Peripatus we meet with a segmental arrangement of tubes, a pair connecting body cavity with the exterior in each segment.

In the Amphioxus there are ninety pairs of tubes, each consisting of two limbs, which open by several apertures into the general body cavity, and by a single ciliated opening externally into the Atrium. The Amphioxus may be regarded as a prototype of the Vertebrata, and the history of development of the excretory organs of some of the higher Craniata, the chick for instance, as described by Sedgwick (Bb 76.), shows that the first stages have a great resemblance to the condition found in the adult Amphioxus. In the chick the cells which give rise to the tubules are found in a great number of segments, and form a long strip of tissue on either side of the body, extending throughout the greater part of its length.

In none of the Craniata are the adult urinary tubes formed from the whole length of this strip. In most, the cells which rise in a few special segments, give origin to the adult kidney. In many Teleosts; the Cod for instance, the urinary tubules are found throughout the greater length of the body, opening into a common longitudinal duct, but the anterior portion close to the head is more developed than the rest, and constitutes the larger part of the kidney. In the higher Classes the anterior tubules do not persist, though present in nearly all for a short period at a very early stage.

According as the anterior, middle, or posterior tubes develope, the structure which they form is called the Pronephros, Mesonephros, or Metanephros. As a rule the kidney represents the Pronephros in the lowest classes, the Mesonephros in the more highly developed, and the Metanephros in the highest. Development takes place from before backwards.

In none of the Craniata is the Pronephros sufficient for excretory purposes, and where it persists there is also to be found some Mesonephros. In Cyclostomata and Teleostei both are found co-existing. In Elasmobranchii the Mesonephros forms the functional kidney, as it also does in Amphibia. The rest of the Craniata including Reptilia, Aves, and Mammalia, often classified together as Amniota, derive their kidneys from the Metanephros. In all three divisions Malpighian bodies are found, but they differ in each; those of the Pronephros are the most primitive, those of the Mesonephros are modified by close relation with the development of the male generative organs, while the Malpighian bodies of the Metanephros are the highest differentiations.

The Malpighian bodies of the Pronephros.

In the Cod fish (Gadus morrhua) the Pronephros, or Head Kidney, is a large irregularly shaped red body situated in front of the Air bladder, and close to the Gills.

On section it appears to be largely composed of round nucleated cells resembling lymphoid tissue lying around the glandular tubules. The Malpighian bodies are not numerous, and are difficult to find. They are very small. Fig. (24) a photomicrograph x700 diameters shows one of the largest. As a rule a number are grouped together round a septum of a thick fibrous nature, and they become more numerous towards the posterior end of the gland. Each is an oval body, and measures about ·06 m.m. from side to side. A glomerulus hangs inside the cavity attached by a rather broad base, which is of a fibrous nature, and continued into the fibrous septum around. The glomerulus always seems to be a dense structure, but this may be partly due to its retraction; it consists of a few capillaries, though these seem very small for the large size of the blood corpuscles. Round its margin can be seen small round cells with round faintly staining nuclei, offering a great contrast to the cells lining Bowman's capsule. The tubule begins opposite the neck of the glomerulus, and its cells are not continued into the capsule, which is lined by a single layer of very flat cells scarcely visible. Between the flat cells and the fibrous tissue surrounding the capsule is a semilunar space, which is generally filled with cells resembling those of the tubules.

Malpighian bodies similar to these are found throughout the kidneys of the cod. Those too of the Haddock (Gadus aeglefinus) are almost identical in structure. One of their chief features is their mode of arrangement in thick fibrous septa. It is also interesting to note the flattened character of the cells of Bowman's capsule, and the rounder cells which cover the tuft.

While the above affords an example from an adult Pronephros, the Malpighian bodies of the Pronephros of early embryos of some of the higher animals are of more importance, as indicating their earliest mode of formation. The "Glomerulus of the Head Kidney" of the chick has been a familiar figure in text books of Embryology since Sedgwick's description, (Bb 77). I have not succeeded in obtaining a preparation to show it, but will mention a few of its characters as

described by Sedgwick. In the chick he found that the Head Kidney was a transitory structure, only present between the 90th & 120th hours of incubation. It consisted of three grooved openings into the peritoneum, but slightly before their formation vascular outgrowths appeared projecting into the body cavity on each side at the root of the Mesentery. Sedgwick at first believed that these formed a vascular ridge, but at a later date he described them as separate structures or glomeruli, and compared them to the glomeruli of the Head Kidneys of the Icthyopsida. Each glomerulus was covered by peritoneal epithelium, and attached by a narrow neck through which passed capillaries from the aorta.
* The External glomeruli were to be found in front of the peritoneal openings of the tubules of the Pronephros. During further development the peritoneal funnels widened considerably, and eventually formed bays, narrow behind, but wide in front, and continuous with the general peritoneal cavity. In these bays other glomeruli developed, and Malpighian bodies thus formed, their cavities being at first part of the peritoneal cavity, but at a later period shut off from it. The epithelium covering the External

and Internal glomeruli was continuous at first, and was part of the peritoneal epithelium, but with the closure of the cavity the two were separated, and the External glomerulus disappeared. Sedgwick concluded that the External glomeruli belonged to primary segmental tubes which never developed.

Sedgwick's description was of special interest in that it showed a close resemblance to the mode of development of the Pronephros in the Cyclostomata, Teleostei, and Amphibia. In the Cyclostomata Balfour (Bb 2.) described the Pronephros as formed from ciliated funnels, which connected the peritoneal cavity with the Segmental duct. On the inner side of the peritoneal openings vascular glomeruli formed, which projected into the body cavity, and were covered with peritoneal epithelium. In Myxine the Pronephros was highly developed, and consisted of ciliated funnels opening into the body cavity, and containing diverticula in which glomeruli formed.

In Teleostei Balfour believed the Pronephros to be formed as a groove in the peritoneal epithelium, which eventually became a funnel. Glomeruli appeared in the funnel, projecting at first into the body cavity, but during further growth the groove deepened, and a partition formed which shut off the cavity.

round the glomerulus from the rest of the body cavity. In this case the cavity of Bowman's capsule was clearly part of the peritoneal cavity, which afterwards became specially shut off for excretory purposes, and both the cells covering the glomerulus, and those lining the capsule were peritoneal in origin.

In Amphibia Balfour described a similar condition, but considered that the formation of a special compartment was incomplete, the cavity round the glomerulus remaining continuous with the body cavity, though partially separated from it.

The structures that have been described are probably homologous, and may be looked upon as rudimentary Malpighian bodies. Most of them are merely transitory, and found only at an early stage of embryonic life. It is doubtful if those of the Head Kidney of the Cod are really part of the true Pronephros. They are probably secondary, and resemble the Malpighian bodies of the Mesonephros. We may consider that the Pronephros in its development affords an example of the most primitive form of what afterwards becomes a definite Malpighian body. It is therefore interesting to note that the glomerulus projects into a cavity, which is part of the general body cavity, its covering is peritoneal epithelium, Bowman's capsule is undeveloped, and its place is occupied by the general lining of the body cavity. In Amphibians a partition appears, but is imperfect; in Teleostei it is complete, and we have the development of Bowman's capsule as a specially enclosed portion of the body cavity, lined with what was actually part of the peritoneal lining.

The Malpighian Bodies of the Mesonephros.

In the Mesonephros the Malpighian bodies reach a high degree of perfection; but show a great variety in the detail of their structure. In some of the lower forms Bowman's capsule still communicates with the body cavity, in others with the ducts of the Testis in the male, in the more highly developed there is no connection with the body cavity, and the Malpighian body resembles that of the Metanephros.

The kidney of the Skate (Raja Batis) is a good example of the Mesonephros. The Malpighian bodies are not numerous, but are very large, varying from .2 to .3 mm in length, about five times as large as those of the Cod. Fig. (25) shows a typical example from the Skate. In shape there is an immense variety, most are very irregular, narrow portions often running some distance between the neighbouring tubules; as a rule the base or attachment of the glomerulus is very broad, in some breadth greatly exceeds length, in others length greatly exceeds breadth. The glomerulus is large and varies in shape in a similar way. In Fig.(25) it is spread out, and individual capillaries can be seen, there is also a dist~~ant~~inct membrane of flat cells with small round nuclei covering the capillaries. Bowman's capsule often shows a definite basement membrane lined with flattened cells; there are usually two openings, but I cannot say if this is always the case, and the cells lining the tubules are prolonged for a short distance into the capsule. One opening is situated opposite the base of the glomerulus, and the other at one side of the base. The tubules are at first narrow, but widen out, and become very large. The cells lining the necks of the tubules are cubical and ciliated. Fig.(26.) shows an opening at the base of the glomerulus. Cilia are found in great numbers in many of the tubules, and appear to be of two kinds. One kind is made up of numerous short cilia, the other of fewer long cilia, or flagella, which look as if a number of the short had united to form a long thick flagellum. Those in the neck of the tubules are more like flagella. In Fig. (25) a few are seen opposite the base of the glomerulus, where tubule begins, the section not showing the lumen of the tube in this case. I have not been able to satisfy myself as to the nature of the second tubule, but according to Balfour it is part of the generative duct from the Testis, or an open canal from the peritoneal cavity in the male; in the female it is from the peritoneal cavity. It would appear therefore that the products from the generative organs of the male pass through some of the Malpighian bodies, while others are in relation to the body cavity. The researches of Balfour on the development of the urinogenital organs of Elasmobranchii are of great interest in showing how these relations have been established. Balfour described the tubules as being formed from mesoblast, and having ciliated funnels opening into the peritoneum, at the deep end of each funnel a Malpighian body appeared. Each primary Malpighian body was connected with peritoneal cavity by a ciliated funnel, and by another tube with the segmental duct at first, the Wolffian duct later. From the primary Malpighian body other secondary Malpighian bodies were formed. He considered that each segment was isolated from the others, and had only one peritoneal funnel, and one communication with the Wolffian duct.

In the kidney of the Skate the Malpighian bodies are grouped together, and some appear almost continuous, but I have not seen a direct connection between their cavities.

In Amphibia the Malpighian bodies are well developed, Bowman showed that the capsule was partly lined by ciliated cells from the neck of the tubule, the presence of flat cells lining the rest of the capsule has long been known. In the kidney of the frog there are also a number of ciliated canals which open into the peritoneal cavity. Balfour believed that these were outgrowths from the neck of the Malpighian body. Nussbaum (Bb 58.) showed that in the adult they opened into the Inferior Vena Cava.

In the male Amphibians part of the urinary canals act as ducts for the Testicular products, the junction of generative ducts with the kidney tubules varying in position in different species.
Heidenhain (Bb 34.) found that in Rana esculenta they

opened into the collecting tubes, Nussbaum (Bb 58.) showed that in Rana temporaria they opened into the necks of the Malpighian bodies. According to Balfour the testicular network of ducts is developed by outgrowths from the primary Malpighian bodies, they do not correspond to the peritoneal funnels. The existence together in the adult kidney of testicular network and peritoneal funnels tends to prove this.

The Mesonephros is well developed in the embryos of some of the Amniota. In the chick it is a large structure, and contains numerous Malpighian bodies. The origin of the tubules has been a matter of dispute. Fürbringer believed them to be formed from peritoneal epithelium, so did Braun. Sedgwick described their origin from the cells of the Intermediate Cell Mass.

The persistence of peritoneal connections with the Malpighian bodies in the Elasmobranches, and their mode of development as shown by Balfour, point strongly to a close resemblance between the Malpighian bodies of the Pro- and Mesonephros. Though never a part of the peritoneal cavity in the Mesonephros, Bowman's capsule is still in communication with it. In Amphibia the communication is interrupted, and the peritoneal funnels, though at first in communication with Bowman's capsule (Balfour), become detached, and open into the Inferior Vena Cava.

The Malpighian bodies of the Metanephros.

The Metanephros forms the permanent kidney of Aves and Mammalia. It arises in the posterior segments of the body behind those of the Mesonephros, and becomes the most highly differentiated of the excretory organs.

The Malpighian bodies vary a great deal in size and appearance, though all are constructed on the same plan. Not only do they vary in different animals, but they show a difference in size in different parts of the kidney of the same animal. Bowman pointed out that the Malpighian bodies which were found nearest the medulla were as a rule larger than those found near the surface of the cortex. The deepest Malpighian bodies are the oldest, and they seem to maintain throughout life the greater size which they acquired during development. Their size however is not altogether dependent on developmental reasons, in most animals they undergo a diminution in size after foetal life is over. This is especially noticeable in Aves, where the Malpighian bodies are very large during development, while in the adult they are much smaller. The alteration in size is probably largely associated with function, and may be regarded as a true Hypertrophy or Atrophy, according as they increase or decrease. In the Human kidney it is not uncommon to meet with both processes. Some of the deep Malpighian bodies in the foetus are larger than any found in the adult kidney, other of the later formed and superficial Malpighian bodies are small, and imperfectly developed at birth, and may remain so for some time in the child, but with increase of function they appear capable of enlargement. These imperfectly formed Malpighian bodies are usually found in positions corresponding to the interlobular septa, their appearance, and the persistence of fibrous tissue around them, led to the belief at one time that they were infarctions.

Bowman's capsule consists of a thin homogenous basement membrane, which is lined by a single layer of cells. The basement membrane is apparently structureless. Rühle (Bb 71.), who has recently examined it very carefully, considers that it is composed of a number of minute fibrils. Ludwig (Bb 52.) believed it to be a mosaic of flattened cells, and other observers by the use of Silver nitrate have come to this conclusion. In the human foetus there is nothing at an early stage to correspond to the stru- -cture which is so noticeable in the adult. The cavity of the capsule is separated from the surrounding connective tissue merely by a layer of cells. In the adult Human kidney the basement membrane bears some resemblance to the elastic lamina of an artery Fig. (28.). Bowman described it as ending round the afferent and efferent arterioles. Rühle considers that it is reflected near them into the glomerulus, where it forms an exceedingly delicate mesh work of fine fibrils. I have often seen it apparently reflected but then disappearing. If the basement membrane is a secretion by the lining membrane, it is most probable that it is continued into the glomerulus, but its development must be influenced by the continual excretion taking place there.

The cells lining Bowman's capsule vary in appearance. The greater part of them are long and flat, and resemble endothelium. In the Human, and most Mammalian kidneys, the whole of the capsule is thus lined. In Birds, and some Mammals e.g. the Mouse, a portion of the capsule is lined by cubical cells, in direct continuation with the flat cells. The transition between the two is sometimes sudden, and at other times more gradual, so that there are cells of an intermediate character present. Where there are cubical cells in Bowman's capsule they are always to be found at the neck of the tubule, and are continuous with the cells lining the convoluted tubule. The cells nearer the base of the glomerulus, i.e., that part of the capsule furthest from the neck of the tubule are always flat. In the Mouse the cubical cells extend over a third or more of Bowman's capsule; they closely resemble the cells of the convoluted tubule, and are probably the same in function. It looks as if this were to be regarded as a Hypertrophy of the convoluted tubule at the expense of Bowman's capsule. In Birds a similar appearance is met with. Fig. (27) is from the kidney of an adult Sparrow. In the Sparrow the Malpighian bodies are very small having a diameter of about ·04 MM. In Fig. (27) which is magnified 1,000 diameters, the capsule is for the most part lined with cubical cells almost identical with the cells of the convoluted tubules. The glomerulus is very small. In this case it appears as if the Malpighian body had undergone changes due to atrophy of its usual function, and had been invaded by the cells of the convoluted tubule converting its function, partly into that of a convoluted tubule. This supposition, if we assume Bowman's theory as true, that the glomerulus excretes fluid, and the cells of the tubules solids, is rendered more likely by the fact that the urine of birds is semi-solid. The cubical cells lining the neck of the capsule in the Mouse have been stated by Klein to be ciliated. I have not seen anything that could be undoubtedly called cilia, appearances something like very fine cilia are sometimes seen, especially in specimens fixed in Corrosive sublimate, whether they are cilia or not I am not prepared to say. Other observers have described cilia in various Mammalian kidneys. Dr. Carlier has recently shown them in the Cat, Sheep, and other Mammals. In the Mesonephric kidney, where the tubules are also the generative ducts, the cilia are well marked, Fig (26), and their presence is easily explained. In the Metanephros it is not so easy to understand why cilia should be present, and they are certainly not very obvious. I have not seen anything resembling cilia in the human foetal kidney.

The convoluted tubule usually leaves Bowman's capsule opposite the base of the glomerulus, but variations occur; and it is often found nearer one side than the other, but never next the base as in the early stages of development, or as in the kidney of the Skate.

The glomerulus is attached by a narrow base consisting chiefly of the afferent and efferent arterioles and the membrane covering them. The capillary loops form lobes, and differ in number and arrangement in different animals. The epithelium covering the glomerulus consists of flat nucleated cells in a single layer, and it dips down between the lobes covering each capillary loop. The relation of the capillaries to the cells covering them is not quite clear; there seems often to be a space between which is exaggerated in some pathological conditions. Fine connective tissue cells and lymphatics have been described, and the mode of development of the glomerulus indicates the possibility of such being present.

The Malpighian body of the Metanephros is surrounded by convoluted tubules. A small amount of connective tissue is also present especially at the base of the glomerulus, but it does not form so prominent a structure as in the Cod, where each Malpighian body is fixed round the periphery of a thick fibrous septum.

Conclusions.

There exists an analogy between most of the animal organs of excretion. The essential parts consist of

1. A cavity in the body.

2. A tube leading from it to the exterior.

In the simplest forms the cavity which is drained by the tube is the coelome or general body cavity. Such an arrangement is found in the Amphioxus. With the greater development of the vascular system a special structure, the glomerulus is formed. The glomerulus at first appears in the general body cavity near the exit of the tubule. This condition is only seen in a short stage of the development of the Pronephros, and no adults remain to show it. In the next stage the glomerulus forms in the mouth of the tubule, which is still in connection with the body cavity. This is found in the Pronephros of the chick, the glomerulus being known as the Internal glomerulus. The condition persists throughout life in the Myxine or Hag Fish.

In Elasmobranchs the cavity in which the glomerulus hangs remains in connection with the body cavity by a tube of more or less length, but some become connected with the Testis, and the urinary tubes take on the action of Vasa deferentia. In Amphibia the kidney is also associated with genital functions, and acts as a Vas deferens. In some Species the testicular canals open into the neck of Bowman's capsule, in others they open into the collecting tubes. In Amphibia the peritoneal connections with the Malpighian bodies become broken off. In Reptiles, Birds, and Mammals Bowman's capsule has no communication with the general body cavity. Its cavity in fact is a specially differentiated one, closely related to, but now distinct from, the general body cavity.

The association of the Urinary with the Genital organs is an interesting one, and increases the complexity of the Mesonephric kidney. In the male the ducts from the Testis open into the general body cavity in the lowest forms, then they open into the specially differentiated cavities the Malpighian bodies, then into the collecting tubes, and in Mammalia their openings have descended to the urethra.

In the kidney of Man it seems only natural to suppose that the cavity of each Malpighian body is a small body cavity specially differentiated for excretory purposes. Its structure supports the assumption. The lining of Bowman's capsule corresponds to the lining of other true body cavities. The cells lining

Bowman's capsule have probably no other function than to form the lining of such a cavity, the thick basement round them in the adult precludes the possibility of their having an excretory function, and gives to the capsule a character more like that of an artery, the basement membrane corresponding to the elastic lamina of the latter. The cells of the tubules though closely allied to the cells lining the capsule are much more highly developed, and take on quite a different structure and function. The epithelium covering the glomerulus is also closely related to the other two, but assumes a different and special character at an early stage. It is further modified to allow of the performance of the excretion of water and some solids, and has no basement membrane, or at least a very fine one with numerous perforations.

The cells lining Bowman's capsule, the cells of the convoluted tubules, and the cells covering the glomerulus, must therefore be regarded as differentiated, and specialised, for the performance of three different functions. Their pathological reactions should also differ, and it is found that they do so. The cells lining Bowman's capsule are the least highly differentiated, and in inflammatory conditions they behave like the endothelium of an artery in Endarteritis. This was long ago taught by Professor Greenfield from a pathological basis; and the embryology, and comparative anatomy of the Malpighian body, give a feasible explanation of what seemed contrary to views generally accepted.

Pathology.

A short consideration of some of the

Pathological Changes in the

Malpighian bodies of the Kidney.

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General Considerations.

In the Kidney there are three important structures which have to be considered in its Pathology. These are

1. The Blood Vessels.
2. The Glandular elements.
3. The Connective Tissue framework.

The Blood Vessels. The Kidney is extremely vascular. Bowman first pointed out that there was a double system of capillaries in the Cortex. The first consisted of the capillary loops forming the Glomerulus, these united to form the efferent arteriole, usually a single thin walled vessel, which almost immediately after leaving the Glomerulus, broke up into the second system, a number of fine capillaries surrounding the convoluted tubes. Ludwig (Bb 52.) showed that the Interlobular arteries each gave off one, and only one, afferent arteriole to each Malpighian body, and that the second system of capillaries, resulting from the breaking up of the efferent arteriole, were distributed among the different portions of the convoluted tubule belonging to that Malpighian body. In other words that each Malpighian body, together with its convoluted tubule, was supplied by a single branch from the Interlobular artery. The development of the kidney gives support to this, in that it shows that the Malpighian body is surrounded by the convolutions of its own tubule, among which the second capillary network is distributed. This fact has a most important bearing in Pathology. It shows that the blood supply to the convoluted tubules is largely dependent on the condition of the capillaries in the glomerulus. Any hindrance to the stream there will bring about a diminution of the blood supply to the convoluted tubules. The diminution will not be quite proportional to the amount of obstruction in the glomerulus, for there exists a certain amount of anastomosis between the capillaries of adjacent convoluted tubules; but if the circulation of a number of neighbouring glomeruli be impaired, there is necessarily an impairment of the blood supply to their convoluted tubes; and as a result of this diminished blood supply, there must be secondary charges produced. The consequences of this vascular arrangement are seen in the frequency with which Infarction occurs in the kidney. They have also been shown experimentally by Professor Greenfield in the production of Infarctions in the dogs' kidney by the injection of Tobacco seeds into the Renal artery. Embolism readily occurs in the afferent arteriole, and in the capillaries of the Glomerulus, and these vessels are also extremely liable to impairment in disease. The glomerulus therefore is a very important factor, changes in its vessels not only inpair its own functions, but they have wider and more general effects, since they interfere with the nutrition and functions of the tubules. Circulation through the vessels of the glomerulus may be hindered by changes inside the vessels, or in their walls, but there may be an additional factor. It is probable that there is a certain amount of connective tissue between the capillary loops of the glomerulus, and in certain inflammatory conditions these cells proliferate, and by their growth compress the vessels. Compression and obliteration of the vessels may also occur in another way, by proliferation of the epithelium lining Bowman's capsule. The results of such obliteration must have, and are found to have, a great influence on the parts of the kidney, that normally receive their blood supply through these glomeruli.

The double capillary system has also another bearing, the importance of which is difficult to estimate. The blood in the second system of capillaries is normally more concentrated owing to the loss of part of its watery element during its passage through the glomerulus. In the nephritis following Scarlatina, and Diptheria, there are probably injurious chemical materials in the blood. These are brought into close relation with the glandular elements in both sets of capillaries. Whether they are excreted through the glomeruli, or pass in a more concentrated form to the convoluted tubules, is undetermined. The changes in Scarlatinal Nephritis would lead one to infer that they acted more especially on the glomeruli at first.

Glomeruli in different parts of the Cortex also appear to be differently affected sometimes; those in the interpyramidal cortex reacting differently to those in the ordinary cortex. The reason of this is not clear.

2. The Glandular elements. These include the epithelial lining of Bowman's capsule, and the covering of the glomerulus, as well as the tubules. In the Development of the kidney it has been shown that all the glandular elements, with the exception of the collecting tubes, are Mesoblastic structures. The collecting tubes are probably Epiblastic. The former constitute the greater part of the cortex, and the Epiblastic tubules the medulla. The Mesoblast or cortex is far more prone to disease than the Med-

-ulla. Sir T. Grainger Stewart (Bb 80.) in his work on "Bright's diseases of the Kidneys" published in 1868 speaking of Cirrhotic kidney said "It is however singular that even when the disease is furthest advanced the cones are comparatively little affected, the cortical substance may be reduced to a very thin layer perhaps one sixth of its natural size, and yet the cones be but slightly wasted." The glandular elements of the cortex are more highly organised, and vascular, and therefore liable to greater changes in disease; but their origin from Mesoblast is probably of importance, such structures showingless power of existence than epiblastic structures when invaded by connective tissue.

In the Malpighian body there are two kinds of epithelium to be noticed, that covering the glomerulus being a more highly differentiated form than that lining Bowman's capsule, and showing a difference in reaction in disease. A third form of epithelium, that lining the neck of the convoluted tubule is also found at times inside Bowman's capsule.

The basement membrane is closely related to the glandular elements, but its exact nature is not clear. It has been supposed to be a homogenous membrane, formed by some process of secretion by the epithelial cells it borders. Others have considered it to be a cellular structure acquiring a fibrous nature, with nuclei imbedded at intervals between the fibres. This view is supported by some common pathological changes, in which the basement membrane appears to be split, and often separated by fibrous tissue, the cells being produced by the proliferation of its nuclei, and the splitting being caused by their further growth. The basement membrane which forms Bowman's capsule often acts in this manner. It shows a remarkable persistence at times, even when the glomerulus has been almost obliterated by cell proliferation inside it. At other times there are appearances suggesting the formation of a new capsule inside the old one, the interval between them being filled with connective tissue, or the one may join the other, and in this way appear as if it had been split up into two or more strands.

There are no pathological changes to support Rühle's view, that the capsule is continued into the glomerulus over the capillary tufts.

3. The Connective Tissue framework. The importance of this has been shown in **development**; and it is of even more importance in Pathology. The connective tissue is small in amount in the cortex, and

scarcely visible in the normal adult kidney. Some persists round the larger blood vessels, and round the Malpighian bodies, especially at the base of the glomerulus; it is probably continued into the glomerulus itself, and binds together the capillaries. The development of the Malpighian body supports such a view. In fact all the structures that form a glomerulus, are so closely related in their origin, that they might be looked as differentiations of the same tissue. Proliferation of connective tissue is soon brought into evidence by the appearance of cells round Bowman's capsule, which have a tendency to arrange themselves in laminae round it. Proliferation inside the glomerulus itself had been described as an evidence of the presence of such cells in that situation. Their proliferation leads to interference with the passage of the blood through the capillaries by pressure on them.

Connective tissue is also found under the capsule, and is more plentiful in the medulla between the large collecting tubes. In all long continued inflammatory changes in the kidney, and especially in Cirrhosis, there is a great increase especially in the cortex of connective tissue, an exaggerated framework of fibrous tissue developes replacing the glandular elements. In the foetal kidney the framework is large in amount and cellular, in the normal adult kidney it is almost non-existent, in Cirrhosis it is large, dense, and fibrous, and constitutes the greater part of the cortex of the kidney.

All three structures, Vascular, Glandular, and Connective tissue have therefore to be considered in the Pathology of the Malpighian body, and from the foregoing remarks it will be seen that alterations in any of these structures will bring about changes of the greatest importance not only in the Malpighian body itself but in the rest of its tubule. The Pathology of the Malpighian body therefore occupies a most important position in the Pathology of the kidney.

Hypertrophy and Atrophy.

It is difficult to determine of some of the changes, which are Pathological and which are Physiological. Since the experiments of Rose Bradford (Bb 7.) it has been recognised that very little healthy kidney substance is required to fulfil the necessary excretory functions of an animal. Bradford found that a quarter of the total amount of kidney was sufficient for ordinary purposes, and he showed the remarkable circumstance that when more than three quarters of the whole kidney substance was removed by operation the excretion of both water and solids was so much increased by the small portion remaining that the animal rapidly emaciated and died. In Pathological conditions of the kidney there are often the most extensive changes with destruction of a great many Malpighian bodies and tubules, yet the out-put of water may be above the normal, and the solid constituents may or may not be decreased.

From a consideration of the development of the kidney it seems extremely improbable that any new Malpighian bodies or tubules should form. The material from which they arise is exhausted at the end of the 8th month of foetal life, and disappears entirely. The subsequent growth of the kidney is essentially a hypertrophy of already formed structures. The hypertrophy or growth appears to be in excess of physiological needs, as if making provision for future contingencies, or for the increased demands on the function occasionally required in health.

In Congenital Cystic kidney it has been alleged that the healthy portion hypertrophies to compensate for the smaller number of functional Malpighian bodies and tubules, and the history of development and mode of subsequent growth of the kidney favour this view. Some Malpighian bodies again in the periphery of the lobules of the normal kidney appear to remain small for some time after birth, such are not found in the adult kidney, and it is very likely that they grow larger with increase of function.

When the kidney is fully formed it is questionable whether Hypertrophy can take place as in the growing kidney. Numerous experiments have been performed. Rosenstein (Bb 68.) in 1871 removed one kidney from an animal, allowed the wound to heal, and after some time killed the animal and compared the two kidneys. He found that there was a slight increase in the epithelium of the tubules, and in the connective tissue. Ribbert (Bb), and Barth (Bb 3.), each came to the conclusion that after removal of one kidney compensatory Hypertrophy occurred in the remaining kidney, the Malpighian bodies increased in size, Bowman's capsule became wider, and the glomerular tufts longer and broader. Ribbert experimented on a large number of animals, and found that in all there was both proliferation of cells, and increase in size of the Malpighian bodies and convoluted tubes. Golgi (Bb 24.) and Sacerdotti (Bb 73.)

performed Nephrectomy on animals, and found that there was active Karyokinesis in the cells of the tubules of the remaining kidney several days after the operation. Golgi (Bb 24) further stated that a similar proliferation of cells took place in some forms of Bright's disease, regeneration by Karyokinesis occurring.

It is not uncommon to find in the Human kidney that part of Bowman's capsule is lined with cubical cells. Fig. (28.) is from a cystic kidney, and shows a well marked basement membrane with cells lining it almost cubical, and gradually enlarging towards the convoluted tube. The same appearance is often met with in some forms of chronic Bright's disease. The question arises. Is this an attempt at Hypertrophy, an attempt to utilise the interior of Bowman's capsule by an ingrowth of cells from the convoluted tubule? In Fig. (28) the enlargement of the cells appears to be more of a swelling of the flattened cells, and the nuclei still preserve some of their flattened character. In other cases one finds well marked cubical cells inside Bowman's capsule as in the normal kidney of the Mouse. The changes which take place in the Malpighian body of birds seem to be of the nature of hypertrophy and atrophy, hypertrophy of the tubule and atrophy of the glomerulus with the result that the Malpighian body in many cases becomes a portion of tubule with scarcely any glomerulus. Fig. (27.).

Mechanical hindrance of the escape of urine from the kidney produces in itself remarkably little alteration in the structure and appearance of the Malpighian bodies. In Hydronephrosis following obstruction of the ureter the Malpighian bodies remain very little altered for a long time. Eventually many become obliterated by fibrous growth. Griffiths (Bb 28.) has recently described the changes as due to a proliferation of the cells lining Bowman's capsule, but he denies that the accompanying interstitial change is the result of interference with the circulation through the capillaries of the glomerulus, a view which he says was advocated by Newman.

Rose Bradford (Bb 8.) has performed a number of experiments on dogs with the object of ascertaining whether obstruction of the Ureter would cause atrophy of the kidney. He ligatured a ureter, and after various periods of from 11 to 40 days removed the ligature, and established a urinary fistula. Some time subsequently he killed the animal, and examined the kidney. As a result of the ligature Hydronephrosis occurred, but after removal of the ligature urine was again excreted, and the kidney rapidly diminished in size, but regained its normal shape though considerably smaller than originally. Very little alteration took place in the Malpighian bodies, the glomerulus was a little shrunken, and the cavity of the capsule wider, but there was no increase of fibrous tissue except round the larger blood vessels, and no proliferation of the cells lining Bowman's capsule. The chief change was in the cells of the convoluted tubules, which had lost their granules, and were smaller and transparent.

In the beginning of December 1898, I removed a wedge shaped portion equal to half the kidney from a cat in the manner described by Bradford (Bb 7.); at the same time one of the stitches in bringing the two ends of the kidney together included the ureter. The animal soon recovered, and the wound healed. In March 1899. a little over three months after the first operation I killed the cat and examined the kidney. The wound had healed with very few surrounding adhesions, and the kidney was less than half the size of the sound kidney. On opening the small kidney a quantity of urine escaped, and the pelvis was found to be dilated. On microscopic examination and comparison with a section of the wedge shaped piece that had been previously removed there was little difference to be seen in the Malpighian bodies. Bowman's capsule was unaltered but the glomerulus was smaller in the hydronephrotic kidney and occupied less of the space. The cells lining the capsule were unaltered. I could not detect any increase of fibrous tissue.

Urinary pressure is a low one, and it seems to produce little effect on the Malpighian bodies; circulation apparently goes on through the glomeruli, and is sufficient to supply the cells of the convoluted tubes. Some additional factor is necessary for the production of the gross forms of atrophy met with in many diseased conditions. This is probably an irritant, and the changes that result are Inflammatory.

Inflammatory Changes.

The Inflammatory lesions of the Malpighian bodies have been classified as Acute, Subacute, and Chronic. Cornil and Brault (Bb 14) applied the name "Glomerulitis" to all these conditions. The name is misleading for the part taken by Bowman's capsule is no less important in its ultimate effects. Professor Greenfield (Bb 26.) divided the changes into those occurring in the capsule itself, those external to it, and those in its interior. These practically resolve themselves into affections of the Blood vessels, epithelium and connective tissue. In acute inflammatory affections of the Kidney the vessels of the glomerulus are soon concerned. Congestion and swelling of the tuft occur very readily. The changes are more marked in some conditions than in others. In the acute infectious diseases especially Scarlatina there are early and important alterations in the vessels. Klein (Bb 44) described these as consisting in a hyaline degeneration of the elastic intima of the minute arteries, especially those of the afferent arterioles of the Malpighian bodies. By swelling of the intima of the capillaries of the glomerulus the circulation through them was greatly interfered with. Klein also described an increase in the nuclei of the muscle cells of the afferent arterioles especially at their points of entrance into the glomeruli. Besides changes in the walls of the vessels there is a diapedesis of leucocytes which accumulate round the base of the glomerulus in many cases of Scarlatinal Nephritis Cornil mentions that the emigration of leucocytes and haemorrhage from the glomerular capillaries is very marked in animals poisoned by Cantharides. The blockage of the capillaries by hyaline thrombi was described by Klein.

Owing to the close relationship between capillaries and the epithelial covering of the glomerulus the changes in them have been much confused, and are not yet quite clear. In most acute inflammatory affections of the glomerulus, and particularly in Scarlatina, there is a great proliferation of nuclei in the tuft. These have been considered to be the nuclei of the capillaries, or of the epithelial covering, or of connective tissue cells lying between the capillaries. Klebs (Bb 43.) was the first to draw general attention to the condition. He gave the name "Glomerulo-nephritis" to the lesions of the Malpighian bodies met with in Scarlatina. Klebs described a great increase in the number of nuclei in the glomerulus and believed that they were the results of the proliferation of connective tissue cells lying between the capillaries. Their increase was to such an extent as to press on the capillaries and prevent circulation through them. Klein (Bb 44.) questioned the accuracy of Klebs's observation; he found that such a proliferation of nuclei was very rare, and was inclined to look on the chief change as a degeneration of the vessels. Hansemann (Bb 31.) adopted Klebs' view, and described proliferation of connective tissue cells in the glomerulus. Kelsch and Kiener (Bb 42.) considered that the proliferation was one of the epithelial envelope covering the glomerulus. Cornil and Brault (Bb 14.) described the change as a proliferation and desquamation of the epithelial cells. According to these authors the nuclei of the epithelial cells dipping between the loops enlarge, the flattened cells become swollen, and a pedicle forms between each one and its attachment, which ultimately becomes separated. Cells are formed in this manner which lie loose inside Bowman's capsule. Langhans (Bb 49.) described the glomerular lesion as a proliferation of the endothelial cells of the capillaries leading to their obliteration. Welch (Bb 88) came to the same conclusion as Langhans and called the condition "Intracapillary Glomerulitis".

Councilman (Bb 15) has recently described the capillary lesions very fully. He found that the majority of the nuclei were those of the capillaries as described by Langhans and Welch, but that some were the result of proliferation of definite connective tissue cells in the glomerulus, there were also a few leucocytes, rarely many, which might be seem in the act of emigration from the vessels into the capsular space. There was a remarkable absence of red cells in all the cases he examined. Hyaline thrombi and partial necrosis of capillaries were found in a few.

There are therefore three opinions on the origin of the nuclei which are so marked a feature of the glomeruli in the early stages of Scarlatinal nephritis. Kelsch and Kiener, Cornil and Brault believe them to be epithelial, Klebs and Hansemann that they are connective tissue, and Langhans, Welch and Councilman that they are endothelial in the main, but a few are connective tisaue. In some cases leucocytes are numerous but their nuclei differ from the small round deeply staining nuclei which are characteristic of the condition. The proliferation of these nuclei varies in amount in different cases but is a marked feature of the Nephritis due to acute infectious diseases, and poisoning by various irritants. They are shown in Fig. (29.) a glomerulus from a cat poisoned by Corrosive Sublimate. In other instances it is not so marked a feature, and it is questionable how much of the change is primary, and how much is a result secondary to alterations in Bowman's capsule.

All the authors above mentioned have described the proliferation of the cells lining Bowman's capsule, but only a few have attached much importance to it. Klebs found a number of angular nuclei lying free in the interior of the capsule in the condition he called Glomerulo-Nephritis. These angular nuclei were usually surrounded by amorphous granular masses which he believed to be the result of the proliferation and degeneration of the capsular epithelium. Klein found a proliferation of nuclei, and the presence of granular material and blood inside the capsule, the thickening of Bowman's capsule and obliteration of glomeruli he ascribed to a general interstitial change. Kelsch (Bb 41.) considered that the change was essentially an interstitial one, and that the thickening of Bowman's capsule was a secondary result. Professor Greenfield (Bb 26.) in 1879 was the first to point out the importance and extent of the cellular proliferation inside the capsule. He showed that the proliferation of these cells was a constant phenomenon not only in Scarlatinal nephritis, but in almost every form. It was more rapid in Scarlatina and led to many important results. The capsule itself sometimes became swollen, but the most common process was a multiplication of the endothelial cells lining it. Similar changes were found by him in the early cirrhotic kidney, the process affecting the more peripheral Malpighian bodies at first, and extending towards the medulla, the glomeruli of certain interlobular arteries being more implicated than those of others. The proliferating cells formed laminae inside the capsule, and eventually became organised tissue; in many cases the opening of the tubule was blocked at an early stage, but in others it remained open, but with the contraction of the fibrous layers the glomerulus atrophied, and in time disappeared, its place being taken by a knot of fibrous tissue. The cells inside the capsule did not always proliferate uniformly, sometimes the growth occurred very rapidly near the base of the glomerulus mechanically interfering with the circulation. Bowman's capsule itself often split up by proliferation of nuclei between its layers, and a concentric pericapsular growth of fibrous tissue was a common accompaniment. The interference with the circulation through the glomeruli led to a loss of part of the function of their convoluted tubes, and at the same time decreased their blood supply. As a consequence the tubules belonging to the affected glomeruli atrophied, and owing to the process affecting those supplied by particular interlobular arteries the kidney showed strips of corresponding atrophied tissue running in from cortex to medulla. In Scarlatinal nephritis proliferation of the cells lining the capsule was often very rapid and early. The capsular epithelium therefore acted very differently to the glomerular epithelium. In the glomerulus there was a proliferation of nuclei as already mentioned, but instead of persisting and increasing the glomerulus gradually shrank and atrophied, the cells of the capsule forming concentric rings and gradually obliterating it.

Langhans (Bb 49.) in the same year described the proliferation of the capsular epithelium as the first change in the Malpighian body, and showed that this growth compressed the vessels.

Cornil and Brault (Bb 14) found that proliferation and desquamation of the cells occurred in Cantharides poisoning, but that it was more marked and important in the subacute inflammations.

Welch (Bb 88.) proposed the name "Desquamitive glomerulitis" for this lesion as against the "Intracapillary glomerulitis" already mentioned. Councilman found it present in all his cases and emphasised its importance.

Friedländer (Bb 19) found that Bowman's capsule was constantly thickened but rarely markedly. In its interior it was common to find sickle shaped masses of flat cells which formed stratified layers round the glomerulus. The epithelial covering of the glomerulus on the other hand rarely increased to any extent. He considered that in the early stages the hindrance to the glomerulur circulation was due, not to outside pressure, but to internal changes in the capillaries.

Proliferation of the cells lining Bowman's capsule is now recognised to be of very common occurrence. It occurs in many cases of irritant poisoning such as by Corrosive Sublimate, in many of the infectious fevers, Cholera, Yellow fever, and especially Scarlatina, in other such as Diptheria it is less marked. The cells for the most part preserve their flattened shape, and form concentric rings inside the capsule. Some of them are free, and show their pointed extremities and flattened nuclei, but the majority remain in apposition, and after a time become organised connective tissue. Bowman's capsule itself shows a remarkable persistence, and is very little altered in many. Fig. (30.) from a section of Human kidney shows the persistence of the basement membrane round the Malpighian bodies with accumulation of cells inside. The kidney was a good example of Subacute Nephritis, non Scarlatinal, but had been too long in Muller's fluid to show detail under high power, the stain by Heidenhain's method has picked out the basement membranes very clearly. The cells are clearly inside the capsule, and are not derived from basement membrane. It is often found that their nuclei have lost the power of staining. Fig. (31.) under a high power shows a similar change, some of the cells are detached, and their characters are very typical. This specimen is from a case of subacute nephritis in which the

Malpighian bodies show all changes from slight thickening to complete obliteration of the glomerulus. Some of the cells have been believed to be derived from the epithelium covering the glomerulus as described by Cornil and Brault. A few may be so derived, but the concentric arrangement and position of the cells indicate that they are capsular in origin. They are often found growing between the lobes of the glomerulus, but they grow in peripherally. Adhesions are of frequent occurrence between the new cells and the capillary tufts. The glomerulus swollen at first, and often showing marked hyaline degeneration, gradually atrophies. The changes can be easily studied in subacute conditions such as seen in Fig. (31.) where the process is slower. Organisation of the newly formed cells takes place and small capillaries appear inside the basement membrane. This latter appears to be often split into layers, some of which enclose numerous cells and capillaries, in many, however, it remains single, and not much thickened. At the same time there is a pericapsular growth of connective tissue, the cells of which become arranged in parallel layers, Fig. (31.), and help to bring about the ultimate atrophy of the Malpighian body.

Another condition is sometimes present in Bowman's capsule in acute forms of Nephritis. It is the presence of degenerated cells from the convoluted tubule. This was found by Councilman in one of his cases, and he gives a diagram illustrating it. Large masses of granular cells were present inside the periglomerular space, and continuous with the cells of the convoluted tubule. I have found the same present in the kidneys of two cats poisoned by Corrosive Sublimate, in both it was a marked feature, some of the spaces being almost filled and the glomerulus flattened against its base. Fig. (29.) shows one of these Malpighian bodies, the indentation of the glomerulus by the cell mass is also seen. It is not the usual lesion described in Corrosive Sublimate poisoning, and appears to be the result of great swelling and detachment of the cells in the neck. The cells lining Bowman's capsule remain in position, and in these instances were little affected. Necrosis of tubular epithelium was very marked in places. Welch (Bb 88.) described the same appearance in Bowman's capsule in the kidneys of rats poisoned by Cantharidin. The cells present no resemblance to the masses which result from proliferation of the cells lining Bowman's capsule, and the lesion probably only occurs in very acute conditions.

The exact relation of changes in the Malpighian bodies to changes in the rest of the kidney is difficult to estimate. As every tubule depends on its Malpighian body for the proper performance of its function, and for much of its blood supply, any lesion in the Malpighian bodies must affect the function and nutrition of the tubules. On the other hand the same cause that effects the capsular lesion will probably produce results directly in other parts of the kidney. Professor Greenfield has shown that in some forms of Cirrhotic Kidney the lesion is one beginning in the most distal Malpighian bodies of certain of the Interlobular arteries, and has advanced as a possible explanation the view that some irritant circulating in the blood has been eliminated by the glomerulus, but remained in a stagnant condition for some time in the distal Bowman's capsule, with the result that the cells have proliferated under irritation.

Once organised tissue has formed inside Bowman's capsule it seems likely that the glomerulus is doomed, contraction gradually occurs, the excretion of urine may continue some time, but eventually the cavity becomes closed and obliterated. In this as in many other kidney changes there is a great variety in the mode of onset and course of the lesion. Some Malpighian bodies are affected early, and ~~some~~ soon disappear, others persist unaltered. In acute conditions too some kidneys show marked changes in the Malpighian bodies, in others they are less evident. The condition termed Glomerulo-nephritis by Klebs while occurring typically in Scarlatinal nephritis appears to be merely an exaggeration of a pathological change which is very common in the kidney in all inflammatory affections.

In these lesions it is seen that the cells lining Bowman's capsule behave, not like the cells of a glandular epithelium, but rather as an endothelium. The changes were aptly compared by Professor Greenfield (Bb 26) to the changes occurring in the inner lining of an artery in endarteritis deformans. The cells covering the glomerulus though possessing a similar anatomical appearance do not act thus, but more after the manner of the tubular cells. I think the reason for this is explained by their development, and by their Comparative anatomy. The cells which line Bowman's capsule, and the convoluted tubules, and cover the glomerulus, arise from Mesoblastic cells closely related to the peritoneal epithelium. The cavity of Bowman's capsule is a specially differentiated body cavity, which in a low form of kidney such as that of the Myxine is a part of the general body cavity, and in the higher forms presents certain close analogies at an early stage of development. The epithelium which lines the cavity flattens very early, and assumes the character of a lining membrane, while the epithelium covering the tuft attains a far higher degree of development, and performs important, and special functions. Though it flattens later on, and resembles the lining cells of the capsule, it is probably a more highly organised structure, differentiated like the cells of the convoluted tubules but in a different manner for excretory purposes. The highly organised structures react to irritation in a different way to endothelium. Their cells easily degenerate and necrose and in catarrhal conditions form different and less persistent masses. On the other hand endothelium proliferates and becomes organised connective tissue. I think we are warranted in regarding the cavity of Bowman's capsule as a specially differentiated body cavity lined by endothelium, and containing a glomerulus of capillaries covered by a special and more highly organised epithelium; the whole structure arising from Mesoblast.

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